```
=> d his

     (FILE 'REGISTRY' ENTERED AT 15:44:35 ON 22 JAN 2004)
                DEL HIS
L1           137 S H[AGV]EGTFTSDVSSYL[EQ]GQAAK[EQ]FIAWLVKGRG/SQSP
L2           128 S ......H[CAGVS][NEDGSCTFMYAVIL][GSCTNQYAVILMF]TFTS[DE][VY]S[SK
L3             6 S L1 AND 37/SQL
L4            12 S L2 AND 37/SQL
L5             6 S L4 NOT L3
L6           393 S H[CAGVS][NEDGSCTFMYAVIL][GSCTNQYAVILMF]TFTS[DE][VY]S[SK]YL[DE
L7            23 S L6 AND 37/SQL
L8            23 S L3-L5,L7
L9            11 S L7 NOT L3-L5

     FILE 'HCAPLUS' ENTERED AT 16:18:02 ON 22 JAN 2004
L10           75 S L3-L5
L11            5 S L9
L12           76 S L10,L11

     FILE 'REGISTRY' ENTERED AT 16:18:34 ON 22 JAN 2004
L13          370 S L1,L2,L6 NOT L8

     FILE 'HCAPLUS' ENTERED AT 16:18:37 ON 22 JAN 2004
L14          166 S L13
L15            1 S WO99-US30395/AP,PRN
L16            1 S US98-113499#/AP,PRN
L17            1 S L15,L16
L18            0 S L17 AND L12
L19            1 S L17 AND L14
                 SEL RN

     FILE 'REGISTRY' ENTERED AT 16:21:18 ON 22 JAN 2004
L20            7 S E1-E7
L21            3 S L20 AND SQL/FA
L22            4 S L20 AND GLUCAGON
L23            4 S L21,L22
L24            1 S L23 AND L1-L9
L25            3 S L23 NOT L24
L26            1 S 89750-14-1
L27            3 S L23 NOT L26

     FILE 'HCAPLUS' ENTERED AT 16:24:00 ON 22 JAN 2004
L28           45 S L27
L29         1102 S L26
L30           30 S L28 AND L29
L31           41 S L28 AND GLUCAGON
L32           28 S L28 AND (PY<=1998 OR PRY<=1998 OR AY<=1998)
L33           26 S L30,L31 AND L32
L34           28 S L32,L33
L35           61 S L12 AND (PY<=1998 OR PRY<=1998 OR AY<=1998)
L36           20 S L35 AND L29
L37           60 S L35 AND GLUCAGON

     FILE 'REGISTRY' ENTERED AT 16:25:47 ON 22 JAN 2004
L38            3 S L20 NOT L23
L39            2 S L38 NOT LYSINE

     FILE 'HCAPLUS' ENTERED AT 16:26:20 ON 22 JAN 2004
L40        13409 S L39
L41            5 S L40 AND L28
L42            1 S L40 AND L12
L43            8 S L40 AND L14
L44            5 S L41-L43 AND (PY<=1998 OR PRY<=1998 OR AY<=1998)
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L45            4 S L28 AND L44
L46            5 S L44,L45
                 E BRADER M/AU
                 E PEKAR A/AU
L47           30 S E3,E4,E10-E12
                 E BRADER M/AU
L48           35 S E4-E6
L49            0 S L47,L48 AND L12
L50            1 S L47,L48 AND L14
L51            1 S L47,L48 AND L28
L52            1 S L50,L51
L53            5 S L46,L52
L54           41 S L34,L36
L55           18 S L54 AND (PHARMACEUT? OR PHARMACOL?)/SC,SX
L56           17 S L54 AND (L27 OR L13)(L)THU/RL
L57           20 S L55,L56
L58           21 S L53,L57


=> fil reg
FILE 'REGISTRY' ENTERED AT 16:31:50 ON 22 JAN 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   21 JAN 2004  HIGHEST RN 640234-51-1
DICTIONARY FILE UPDATES:  21 JAN 2004  HIGHEST RN 640234-51-1

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2003

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

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L27  ANSWER 1 OF 3  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   194551-05-8  REGISTRY
CN   Glycine, L-histidyl-L-valyl-L-α-glutamylglycyl-L-threonyl-L-
     phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-
     L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-
     L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-
     tryptophyl-L-leucyl-L-valyl-L-lysylglycyl-L-arginyl- (9CI)  (CA INDEX
     NAME)
OTHER NAMES:
CN   112: PN: WO0198331 TABLE: 1 claimed protein sequence
CN   1: PN: WO0012116 SEQID: 4 claimed protein
CN   1: PN: WO0247715 SEQID: 1 claimed sequence
CN   29: PN: WO03014318 SEQID: 26 claimed sequence
CN   54: PN: WO0198331 TABLE: 1 claimed protein sequence
CN   59: PN: WO03058203 SEQID: 59 unclaimed sequence
CN   5: PN: WO0155213 SEQID: 5 claimed sequence
CN   6: PN: WO0247716 PAGE: 59 claimed protein
CN   Glucagon-related peptide 1 (synthetic Val-isoform)
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FS PROTEIN SEQUENCE; STEREOSEARCH
SQL **31**

PATENT ANNOTATIONS (PNTE):

Sequence Source	Patent Reference
Not Given	WO2000012116 claimed SEQID 4
	WO2001055213 claimed SEQID 5
	WO2001098331 claimed TABLE 1
	WO2002047715 claimed SEQID 1
	WO2002047716 claimed PAGE 59

SEQ 1 HVEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

RELATED SEQUENCES AVAILABLE WITH SEQLINK
MF C153 H232 N40 O47
SR CA
LC STN Files: CA, CAPLUS, USPAT2, USPATFULL

Absolute stereochemistry.

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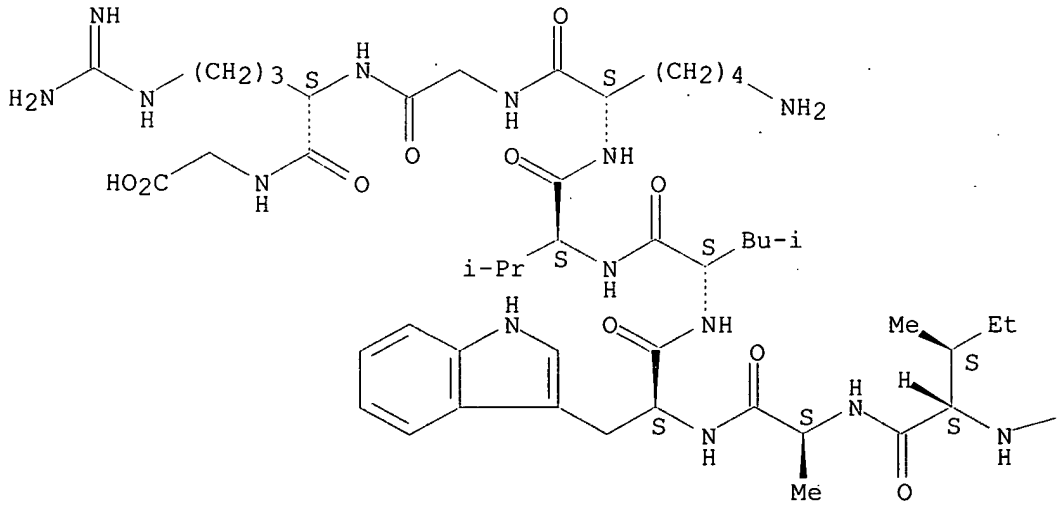

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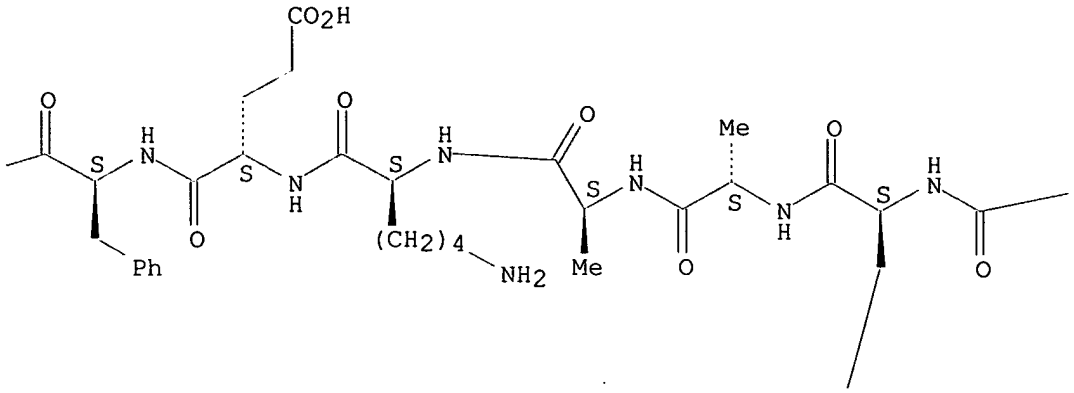

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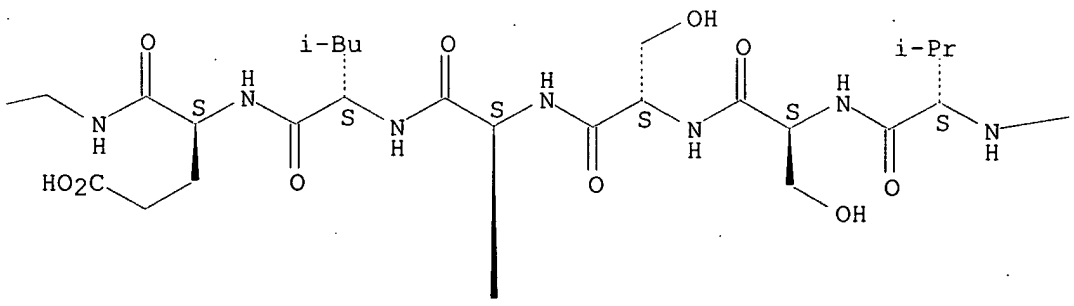

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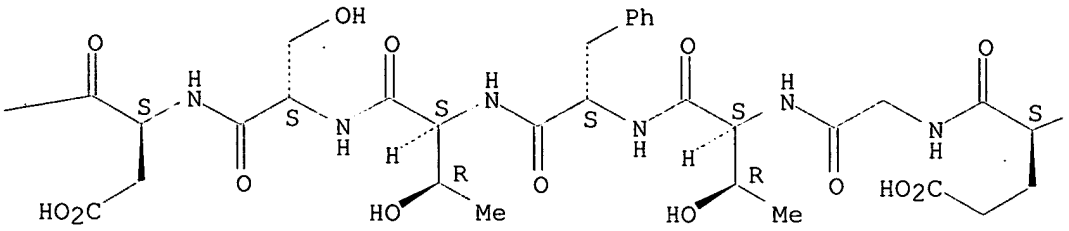

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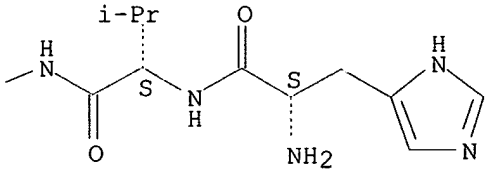

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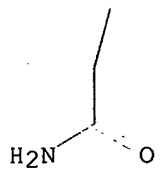

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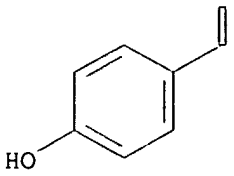

22 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
22 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:35961

REFERENCE 2: 139:333128

REFERENCE 3: 139:302514

REFERENCE 4: 139:174286

REFERENCE 5: 139:80301

REFERENCE 6: 139:26621

REFERENCE 7: 138:298125

REFERENCE 8: 138:180738

REFERENCE 9: 137:52370

REFERENCE 10: 137:42097

L27 ANSWER 2 OF 3 REGISTRY COPYRIGHT 2004 ACS on STN
RN **127650-06-0** REGISTRY
CN L-Lysine, L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **Glucagon-related peptide 1 (Rana catesbeiana), 3-L-glutamic acid-10-L-valine-16-glycine-17-L-glutamine-23-L-isoleucine-24-L-alanine-27-L-valine-29-deglycine-30-de-L-arginine-31-de-L-proline-32-de-L-lysine-**
OTHER NAMES:
CN 26: PN: WO03014318 SEQID: 23 claimed sequence
CN 27: PN: WO0009666 SEQID: 4 unclaimed sequence
CN 3: PN: WO0028067 PAGE: 16 unclaimed protein
CN 6: PN: US20030221201 SEQID: 7 unclaimed sequence
CN **Glucagon-like peptide I(7-34)**
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL **28**

PATENT ANNOTATIONS (PNTE):

Sequence Source	Patent Reference
Not Given	WO2000009666 unclaimed SEQID 4
	WO2000028067

|unclaimed
|PAGE 16

SEQ 1 HAEGTFTSDV SSYLEGQAAK EFIAWLVK

RELATED SEQUENCES AVAILABLE WITH SEQLINK
DR 186462-39-5, 270056-56-9
MF C141 H210 N34 O44
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL

Absolute stereochemistry.

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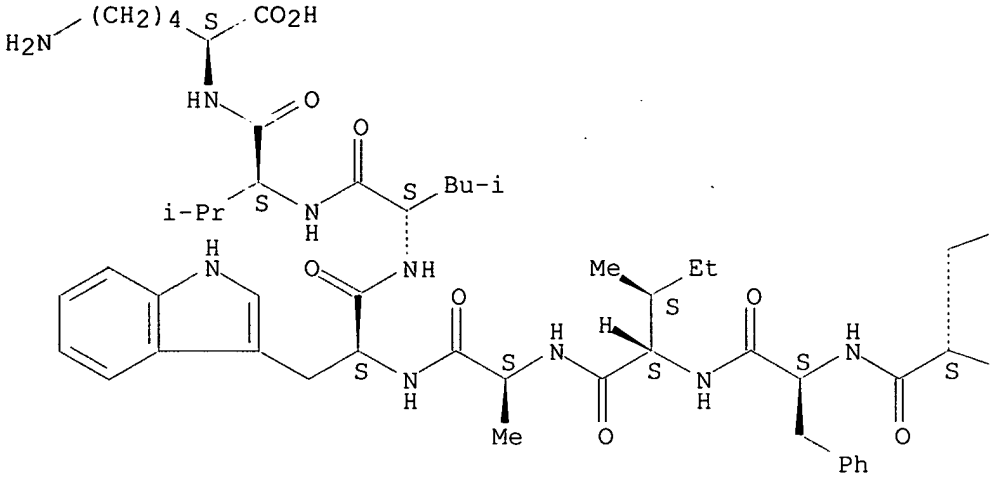

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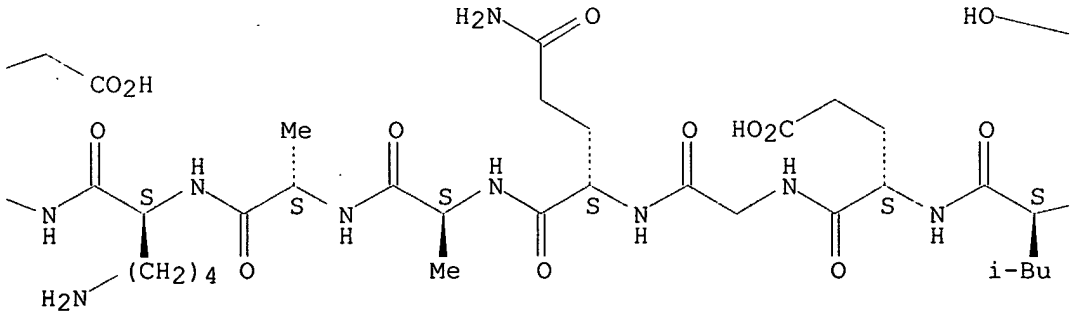

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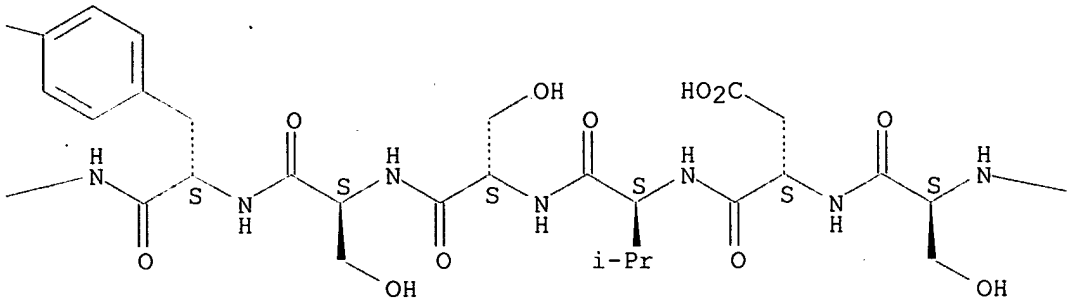

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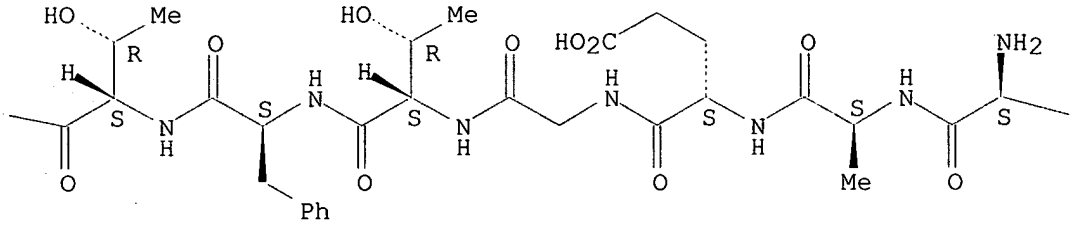

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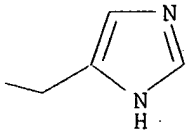

17 REFERENCES IN FILE CA (1907 TO DATE)
18 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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REFERENCE 2: 138:180738

REFERENCE 3: 135:376777

REFERENCE 4: 135:200441

REFERENCE 5: 133:64006

REFERENCE 6: 133:3760

REFERENCE 7: 132:175839

REFERENCE 8: 130:247048

REFERENCE 9: 129:23726

REFERENCE 10: 126:127176

L27 ANSWER 3 OF 3 REGISTRY COPYRIGHT 2004 ACS on STN
RN **123475-28-5** REGISTRY
CN Glycine, L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-lysyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **Glucagon-related peptide 1 (Rana catesbeiana), 3-L-glutamic acid-10-L-valine-16-glycine-17-L-glutamine-23-L-isoleucine-24-L-alanine-27-L-valine-30-de-L-arginine-31-de-L-proline-32-de-L-lysine-**
OTHER NAMES:
CN 26: PN: WO0009666 SEQID: 3 unclaimed sequence
CN 27: PN: WO03014318 SEQID: 24 claimed sequence
CN 7: PN: US20030221201 SEQID: 8 unclaimed sequence
CN **Glucagon-like peptide I(7-35)**
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL **29**

PATENT ANNOTATIONS (PNTE):
Sequence |Patent

Source	Reference
Not Given	WO2000009666
	unclaimed
	SEQID 3

SEQ 1 HAEGTFTSDV SSYLEGQAAK EFIAWLVKG

RELATED SEQUENCES AVAILABLE WITH SEQLINK
DR 186462-38-4
MF C143 H213 N35 O45
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL

Absolute stereochemistry.

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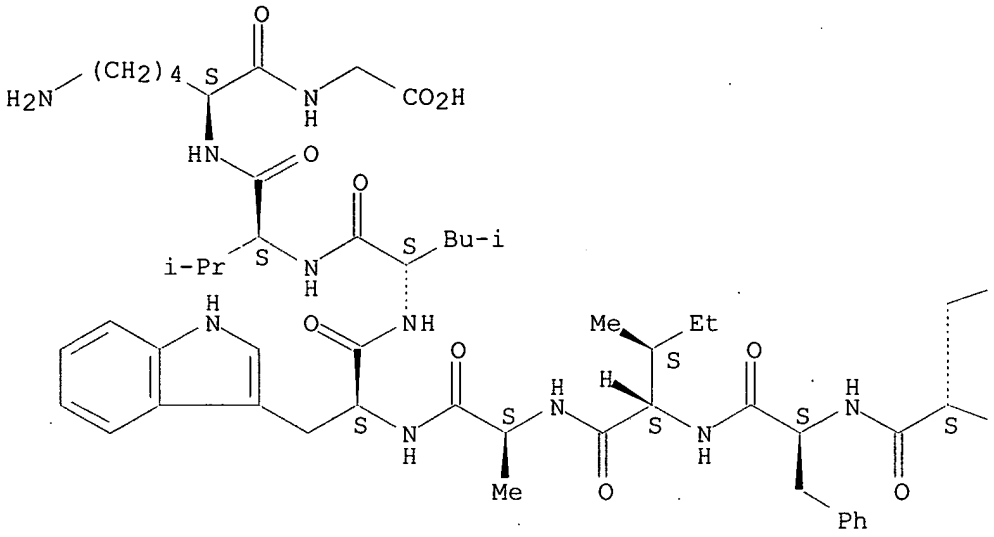

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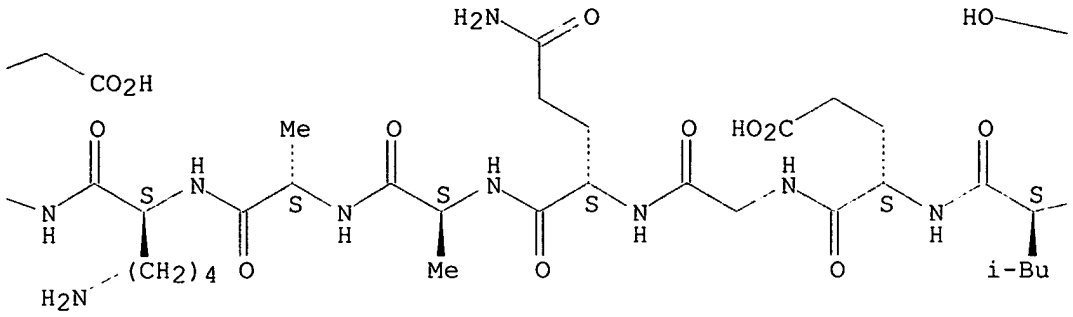

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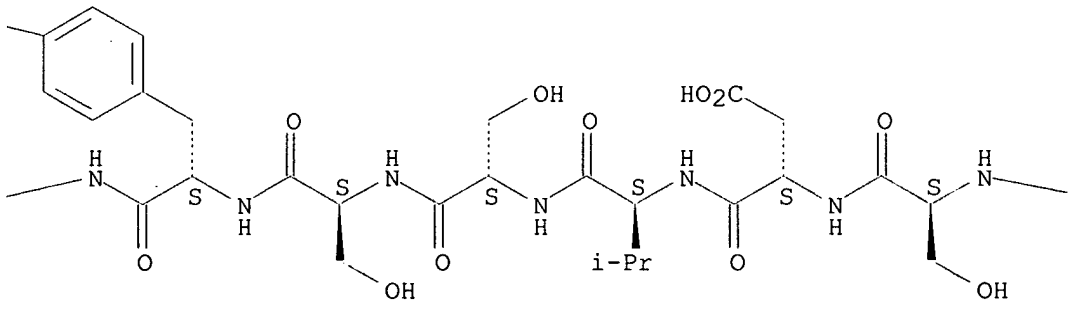

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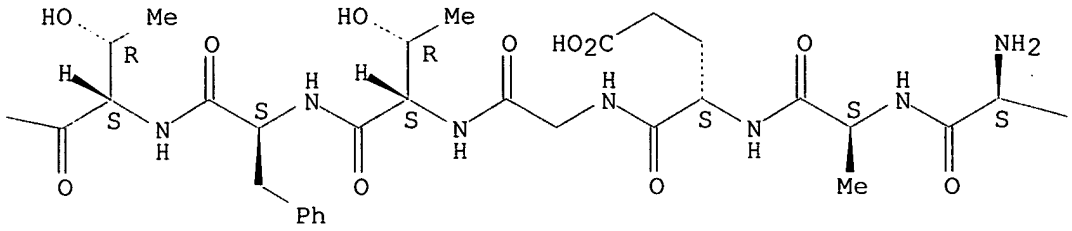

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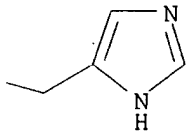

21 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
22 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:8762

REFERENCE 2: 138:180738

REFERENCE 3: 135:273221

REFERENCE 4: 135:200441

REFERENCE 5: 135:122756

REFERENCE 6: 133:64006

REFERENCE 7: 132:175839

REFERENCE 8: 130:247048

REFERENCE 9: 129:23726

REFERENCE 10: 128:244341

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L26 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN **89750-14-1** REGISTRY
CN Glucagon-like peptide I (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Glucagon-related peptide I
OTHER NAMES:
CN GLP 1
CN Glucagon-related peptide 1
MF Unspecified
CI COM, MAN
LC STN Files: AGRICOLA, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CIN, EMBASE, IPA, MEDLINE, MRCK*, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)

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REFERENCE 6: 140:28048

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REFERENCE 10: 140:23485

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L39 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2004 ACS on STN
RN **9002-92-0** REGISTRY
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OTHER NAMES:
CN α-Dodecyl-ω-hydroxypoly(oxy-1,2-ethanediyl)
CN α-Dodecyl-ω-hydroxypoly(oxyethylene)
CN 40L
CN 40L (polyether)
CN Actinol L 3

CN Actinol L 7
CN Adeka Carpol MBF 100
CN Adekatol LA 1275
CN Adekatol LA 50
CN Aethoxysklerol
CN Aetoxisclerol
CN Akyporox RLM 160
CN Akyporox RLM 22
CN Akyporox RLM 230
CN Akyporox RLM 40
CN Aldosperse L 9
CN Alkasurf LAN 1
CN Alkasurf LAN 3
CN Arapol 0712
CN Atlas G 2133
CN Atlas G 3705
CN Atlas G 3707
CN Atlas G 4829
CN Atmer 135
CN B 205
CN Base LP 12
CN BL 2
CN BL 9
CN BL 9 (polyglycol)
CN BL 9EX
CN Blaunon EL 1503P
CN Blaunon EL 1509
CN Brij 22
CN Brij 23
CN Brij 30
CN Brij 30ICI
CN Brij 30SP
CN Brij 35
CN Brij 35L
CN Brij 35P
CN Brij 36T
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CN Chimipal AE 3
CN Cimagel
CN Conion 275-100
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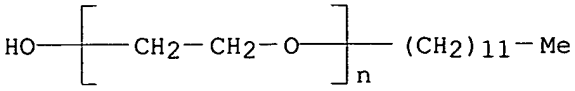
CI PMS, COM
PCT Polyether

LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DETHERM*, DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IMSCOSEARCH, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK*, MSDS-OHS, PDLCOM*, PROMT, RTECS*, TOXCENTER, ULIDAT, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, TSCA**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



8589 REFERENCES IN FILE CA (1907 TO DATE)
205 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
8606 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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REFERENCE 5: 140:47037

REFERENCE 6: 140:35038

REFERENCE 7: 140:17758

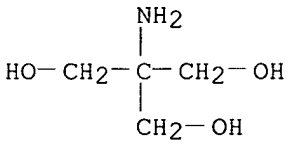
REFERENCE 8: 140:14524

REFERENCE 9: 140:9848

REFERENCE 10: 140:8788

L39 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2004 ACS on STN
RN **77-86-1** REGISTRY
CN 1,3-Propanediol, 2-amino-2-(hydroxymethyl)- (8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
CN 2-Amino-2-(hydroxymethyl)propane-1,3-diol
CN 2-Amino-2-methylol-1,3-propanediol
CN Addex-Tham
CN Aminotri(hydroxymethyl)methane
CN Aminotrimethylolmethane
CN Aminotris(hydroxymethyl)methane
CN Methanamine, 1,1,1-tris(hydroxymethyl)-
CN NSC 103026
CN NSC 6365
CN NSC 65434
CN Pehanorm
CN Sarkosyl
CN Talatrol
CN TAM
CN TAM (buffering agent)
CN THAM
CN Tri Amino
CN Tri(hydroxymethyl)methylamine
CN Trigmo base

CN Triladyl
CN Trimethylolaminomethane
CN Tris
CN Tris (buffering agent)
CN Tris Amino
CN Tris Amino Crystal
CN Tris buffer
CN Tris(hydroxymethyl)aminomethane
CN Tris(hydroxymethyl)methanamine
CN Tris(hydroxymethyl)methylamine
CN Tris(methylolamino)methane
CN Tris-steril
CN Trisamin
CN Trisamine
CN Trisaminol
CN Trispuffer
CN Trizma
CN Trometamol
CN Trometamole
CN Tromethamine
CN Tromethane
CN Tromethanmin
CN Tutofusin tris
FS 3D CONCORD
DR 25149-07-9, 68755-45-3, 83147-39-1, 108195-86-4
MF C4 H11 N O3
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DETHERM*, DIOGENES, DRUGU, EMBASE, GMELIN*, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PIRA, PROMT, RTECS*, SPECINFO, TOXCENTER, USAN, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4817 REFERENCES IN FILE CA (1907 TO DATE)
296 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
4828 REFERENCES IN FILE CAPLUS (1907 TO DATE)
71 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 140:52154

REFERENCE 2: 140:47577

REFERENCE 3: 140:47374

REFERENCE 4: 140:43272

REFERENCE 5: 140:38376

REFERENCE 6: 140:38262

REFERENCE 7: 140:35957

REFERENCE 8: 140:30264

REFERENCE 9: 140:23631

REFERENCE 10: 140:19605

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FILE COVERS 1907 - 22 Jan 2004 VOL 140 ISS 4
FILE LAST UPDATED: 21 Jan 2004 (20040121/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all tot 158

L58 ANSWER 1 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:1013109 HCAPLUS
ED Entered STN: 31 Dec 2003
TI In vivo production and delivery of insulinotropin or erythropoietin for anemia gene therapy
IN Selden, Richard F.; Treco, Douglas; Heartlein, Michael W.
PA Transkaryotic Therapies, Inc., USA
SO U.S., 26 pp., Cont.-in-part of U.S. Ser. No. 446,912.
CODEN: USXXAM
DT Patent
LA English
IC ICM C12N015-85
ICS C07H021-04
NCL 435325000; 435455000; 435461000; 435352000; 435366000; 435360000; 435357000; 435069100; 435069400; 435070100
CC 1-1 (**Pharmacology**)
Section cross-reference(s): 3, 2, 13
FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6670178	B1	20031230	US 2000-552709	20000419 <--
	EP 750044	A2	19961227	EP 1996-202037	19921105 <--
	EP 750044	A3	19970115		
	EP 750044	B1	20020807		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, SE				
	EP 1221477	A2	20020710	EP 2001-204619	19921105 <--

EP 1221477 A3 20020724
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, IE
JP 2003174897 A2 20030624 JP 2002-359926 19921105 <--
US 5994127 A 19991130 US 1994-334455 19941104 <--
US 6048524 A 20000411 US 1995-446909 19950522 <--
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US 2002155597 A1 20021024 US 1999-328130 19990608 <--
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PRAI US 1992-911533 A1 19920710 <--
US 1994-334455 A3 19941104 <--
US 1995-446912 A2 19950522 <--
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AB The present invention relates to transfected primary and secondary somatic cells of vertebrate origin, particularly mammalian origin, transfected with exogenous genetic material (DNA) that encodes erythropoietin or an insulinotropin (e.g., derivs. of **glucagon**-like peptide 1 (GLP-1)), methods by which primary and secondary cells are transfected to include exogenous genetic material encoding erythropoietin or an insulinotropin, methods of producing clonal cell strains or heterogenous cell strains that express erythropoietin or an insulinotropin, methods of gene therapy, in which the transfected primary or secondary cells are used, and methods of producing antibodies using the transfected primary or secondary cells. The present invention includes primary and secondary somatic cells, such as fibroblasts, keratinocytes, epithelial cells, endothelial cells, glial cells, neural cells, formed elements of the blood, muscle cells, other somatic cells that can be cultured, and somatic cell precursors, which have been transfected with exogenous DNA encoding EPO or an insulinotropin that is stably integrated into their genomes or is expressed in the cells episomally. In particular, vectors expressing human erythropoietin (plasmid pXEPO1 and pE3neoEPO) and **glucagon** insulinotropin derivs., such as GLP-1 (7-37, or 7-36; pXGLP1) in fusion with a signal peptide, such as 26-amino acid signal peptide of human growth hormone under the control of mouse metallothionein promoter are constructed. These vectors are used to transfect primary or secondary skin fibroblasts from human and rabbit which demonstrates stable secreted expression of erythropoietin or insulinotropin. The stably transfected rabbit fibroblasts clone is further used in mouse implantation and expression of biol. active human erythropoietin in implanted mice are observed Specifically, it clearly demonstrates that normal skin fibroblasts that have been genetically engineered to express and secrete HEPO can: (1) survive in vivo to deliver HEPO to an animal's systemic circulation for up to 2 mo, and (2) the hEPO produced is biol. functional, serving to prevent the drop in hematocrit observed in the frequently bled control animals, and resulting in a net increase in HCT even when animals were challenged with a bleeding schedule that produces an anemic response in control animals.

ST insulinotropin erythropoietin transformation vector somatic cell anemia gene therapy; erythropoietin transformation vector somatic cell anemia gene therapy

IT Mutation
(deletion, GLP-1 insulinotropin derivs. containing; in vivo production and delivery of insulinotropin or erythropoietin for anemia gene therapy)

IT Hematocrit
(enzyme assay of; in vivo production and delivery of insulinotropin or

erythropoietin for anemia gene therapy)
IT Skin
(fibroblast of, transformation of; in vivo production and delivery of insulinotropin or erythropoietin for anemia gene therapy)
IT Liver
(hepatocyte, transformation of; in vivo production and delivery of insulinotropin or erythropoietin for anemia gene therapy)
IT Anemia (disease)
Blood cell
Gene therapy
Transformation, genetic
Transplant and Transplantation
(in vivo production and delivery of insulinotropin or erythropoietin for anemia gene therapy)
IT Mutation
(insertion, GLP-1 insulinotropin derivs. containing; in vivo production and delivery of insulinotropin or erythropoietin for anemia gene therapy)
IT Skin
(keratinocyte, transformation of; in vivo production and delivery of insulinotropin or erythropoietin for anemia gene therapy)
IT Plasmid vectors
(pE3neoEPO, human EPO gene on; in vivo production and delivery of insulinotropin or erythropoietin for anemia gene therapy)
IT Plasmid vectors
(pXEPO1, human EPO gene on; in vivo production and delivery of insulinotropin or erythropoietin for anemia gene therapy)
IT Plasmid vectors
(pXGLP1, human GLP-1 (7-37 or 36) on; in vivo production and delivery of insulinotropin or erythropoietin for anemia gene therapy)
IT Secretion (process)
(protein, directed by signal peptide; in vivo production and delivery of insulinotropin or erythropoietin for anemia gene therapy)
IT Signal peptides
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(recombinant erythropoietin or insulinotropin containing; in vivo production and delivery of insulinotropin or erythropoietin for anemia gene therapy)
IT Genetic markers
(selectable, insulinotropin or EPO vector containing; in vivo production and delivery of insulinotropin or erythropoietin for anemia gene therapy)
IT Gene, animal
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(selection marker for nutritional auxotrophy; in vivo production and delivery of insulinotropin or erythropoietin for anemia gene therapy)
IT Cytotoxic agents
Drug resistance
(selection marker for; in vivo production and delivery of insulinotropin or erythropoietin for anemia gene therapy)
IT Human
Rabbit
(skin fibroblast of; in vivo production and delivery of insulinotropin or erythropoietin for anemia gene therapy)
IT Human
Mammalia
(somatic cell of; in vivo production and delivery of insulinotropin or erythropoietin for anemia gene therapy)
IT Animal cell
(somatic, transformation of; in vivo production and delivery of insulinotropin or erythropoietin for anemia gene therapy)
IT Mutation
(substitution, GLP-1 insulinotropin derivs. containing; in vivo production and

delivery of insulinotropin or erythropoietin for anemia gene therapy)

IT Endothelium
Epithelium
Fibroblast
Muscle
Nerve
Neuroglia
(transformation of; in vivo production and delivery of insulinotropin or erythropoietin for anemia gene therapy)

IT 11096-26-7P, Erythropoietin **89750-14-1DP**, GLP-1, insulinotropin derivs. **106612-94-6DP**, derivs. 118549-37-4DP, Insulinotropin, derivs. **123475-28-5DP**, derivs. **127650-06-0DP**, **Glucagon**-like peptide I(7-34), derivs.
RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(in vivo production and delivery of insulinotropin or erythropoietin for anemia gene therapy)

IT 639540-58-2, 1: PN: US6670178 SEQID: 1 unclaimed DNA 639540-59-3, 2: PN: US6670178 SEQID: 2 unclaimed DNA 639540-60-6, 3: PN: US6670178 SEQID: 3 unclaimed DNA 639540-61-7, 4: PN: US6670178 SEQID: 4 unclaimed DNA 639540-62-8, 5: PN: US6670178 SEQID: 5 unclaimed DNA 639540-63-9, 6: PN: US6670178 SEQID: 6 unclaimed DNA 639540-64-0, 7: PN: US6670178 SEQID: 7 unclaimed DNA 639540-65-1, 8: PN: US6670178 SEQID: 8 unclaimed DNA
RL: PRP (Properties)
(unclaimed nucleotide sequence; in vivo production and delivery of insulinotropin or erythropoietin for anemia gene therapy)

RE.CNT 150 THERE ARE 150 CITED REFERENCES AVAILABLE FOR THIS RECORD

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L58 ANSWER 2 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:300601 HCAPLUS
DN 138:298126
ED Entered STN: 18 Apr 2003
TI Compositions and methods for treating peripheral vascular disease with GLP-1 compounds
IN Hathaway, David R.; Coolidge, Thomas R.
PA USA
SO U.S. Pat. Appl. Publ., 12 pp., Cont.-in-part of U.S. Ser. No. 851,738.
CODEN: USXXCO
DT Patent
LA English
IC ICM A61K038-17
ICS A61K038-06; A61K031-70; A61K038-44; A61K031-355; A61K031-405; A61K033-00
NCL 514012000; 424094400; 514018000; 514419000; 514458000; 514023000; 424722000
CC 2-6 (Mammalian Hormones)
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	US 2003073626	A1	20030417	US 2002-91258	20020305	
	US 6284725	B1	20010904	US 1999-302596	19990430	<--
	US 2002055460	A1	20020509	US 2001-851738	20010509	<--
PRAI	US 1999-302596	A3	19990430			
	US 2001-851738	A2	20010509			
	US 1998-103498P	P	19981008	<--		

AB The present invention relates to methods of treating intermittent claudication comprising administering glucagon-like peptide-1 (GLP-1) mols. to subjects suffering therefrom. A method of treating or preventing skeletal muscle injury caused by ischemia and/or reperfusion in a subject comprising the step of administering a therapeutically effective amount of GLP-1 mol. is also claimed. The subject can also be administered free radical scavengers, glucose, or potassium. The GLP-1 compound is administered by an infusion pump or by s.c. injection of a slow-release formulation.
ST peripheral vascular disease treatment GLP1; intermittent claudication treatment GLP1
IT Anti-ischemic agents
Cardiovascular agents
Human
(compns. and methods for treating peripheral vascular disease with GLP-1 compds.)
IT Radical scavengers
(compns. and methods for treating peripheral vascular disease with GLP-1 compds. in combination with radical scavengers)
IT Heart, disease
(infarction; compns. and methods for reducing heart infarction by treatment with GLP-1 compds.)
IT Drug delivery systems
(infusion pumps; compns. and methods for treating peripheral vascular disease with GLP-1 compds.)
IT Reperfusion
(injury; compns. and methods for treating peripheral vascular disease

with GLP-1 compds.)
IT Artery, disease
(intermittent claudication; compns. and methods for treating peripheral vascular disease with GLP-1 compds.)
IT Heart, disease
Muscle, disease
(ischemia; compns. and methods for treating peripheral vascular disease with GLP-1 compds.)
IT Blood vessel, disease
(peripheral; compns. and methods for treating peripheral vascular disease with GLP-1 compds.)
IT Drug delivery systems
(slow-release; compns. and methods for treating peripheral vascular disease with GLP-1 compds.)
IT **510788-25-7**
RL: PRP (Properties)
(Unclaimed; compns. and methods for treating peripheral vascular disease with GLP-1 compds.)
IT **89750-14-1D**, Glucagon-like peptide I, compds. **106612-94-6**
, Human GLP-1(7-37) 107444-51-9 141732-76-5, Exendin-4 161748-29-4
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(compns. and methods for treating peripheral vascular disease with GLP-1 compds.)
IT 50-99-7, D-Glucose, biological studies 7440-09-7, Potassium, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. and methods for treating peripheral vascular disease with GLP-1 compds. in combination with glucose and potassium)
IT 70-18-8, Glutathione, biological studies 73-31-4, Melatonin 1406-18-4, Vitamin E 9054-89-1, Superoxide dismutase
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. and methods for treating peripheral vascular disease with GLP-1 compds. in combination with radical scavengers)
IT 510788-20-2 510788-21-3 510788-22-4 510788-23-5 510788-24-6 510788-26-8
RL: PRP (Properties)
(unclaimed protein sequence; compns. and methods for treating peripheral vascular disease with GLP-1 compds.)
IT 176253-51-3 305790-37-8
RL: PRP (Properties)
(unclaimed sequence; compns. and methods for treating peripheral vascular disease with GLP-1 compds.)

L58 ANSWER 3 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:721487 HCAPLUS
DN 135:273221
ED Entered STN: 03 Oct 2001
TI Preparation of lipophilic human **glucagon**-like peptide-1 derivatives with protracted action profiles
IN Knudsen, Liselotte; Huusfeldt, Per Olaf; Nielsen, Per Franklin; Kaarsholm, Niels C.; Olsen, Helle Birk; Bjorn, Soren Erik; Pedersen, Freddy Zimmerdahl; Madsen, Kjeld
PA Novo Nordisk A/s, Den.
SO U.S., 136 pp., Cont.-in-part of U.S. Ser. No. 38,432, abandoned.
CODEN: USXXAM
DT Patent
LA English
IC A61K039-16; A61K038-26; C07K014-00; C07K146-05
NCL 514012000
CC 34-3 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): **1, 63**

FAN.CNT 12

	PATENT NO.	KIND	DATE		APPLICATION NO.	DATE	
PI	US 6268343	B1	20010731		US 1999-258750	19990226	<--
	WO 9808871	A1	19980305		WO 1997-DK340	19970822	<--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM						
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG						
	JP 2001011095	A2	20010116		JP 2000-152778	19970822	<--
	ZA 9707791	A	19980302		ZA 1997-7791	19970829	<--
	ZA 9707828	A	19980302		ZA 1997-7828	19970901	<--
	ZA 9901571	A	19990902		ZA 1999-1571	19990226	<--
	US 2001011071	A1	20010802		US 1999-398111	19990916	<--
	US 6458924	B2	20021001				
	US 2002025933	A1	20020228		US 2001-908534	20010718	<--
	US 2003199672	A1	20031023		US 2002-285079	20020819	<--
PRAI	DK 1996-931	A	19960830	<--			
	DK 1996-1259	A	19961108	<--			
	DK 1996-1470	A	19961220	<--			
	US 1997-36255P	P	19970124	<--			
	US 1997-36226P	P	19970125	<--			
	WO 1997-DK340	A2	19970822	<--			
	US 1997-918810	B2	19970826	<--			
	DK 1998-263	A	19980227	<--			
	DK 1998-264	A	19980227	<--			
	DK 1998-268	A	19980227	<--			
	DK 1998-272	A	19980227	<--			
	DK 1998-274	A	19980227	<--			
	US 1998-38432	B2	19980311	<--			
	DK 1998-508	A	19980408	<--			
	DK 1998-509	A	19980408	<--			
	US 1998-82478P	P	19980421	<--			
	US 1998-82480P	P	19980421	<--			
	US 1998-84357P	P	19980421	<--			
	US 1998-82802P	P	19980423	<--			
	US 1997-35904P	P	19970124	<--			
	US 1997-35905P	P	19970124	<--			
	JP 1998-511183	A3	19970822	<--			
	US 1997-922200	B2	19970902	<--			
	DK 1998-271	A	19980227	<--			
	EP 1998-610006	A	19980313	<--			
	US 1998-78422P	P	19980318	<--			
	DK 1998-507	A	19980408	<--			
	US 1998-82479P	P	19980421	<--			
	US 1998-85789P	P	19980518	<--			
	US 1999-258187	B1	19990225				
	US 1999-258750	A2	19990226				
	US 1999-265141	A2	19990308				
	US 1999-398111	A1	19990916				

OS MARPAT 135:273221

AB The present invention relates to human **glucagon**-like peptide-1 (GLP-1) derivs. having a lipophilic substituent, compns. containing these derivs., and to methods for their preparation A claimed compound is His-Ala-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Val-Ser-Ser-Tyr-Leu-Glu-Gly-Gln-Ala-Ala-Lys-Glu-Phe-Ile-Ala-Trp-Leu-Val-Arg-Gly-Arg-Gly. Thus, coupling of GLP-1(7-37)-OH with Me(CH2)12CO-Glu(OSu)-OCMe3 (Su = succinimidyl) (preparation given), followed by deesterification with CF3CO2H and chromatog. purification

gave 8% bis-adduct Lys[Me(CH2)12CO-γ-Glu]26,34-GLP-1(7-37)-OH.
Several prepared lipophilic GLP-1 analogs were tested for protracted plasma concentration in pigs and were found to be much more persistent than GLP-1(7-37).
In addition, the time of peak plasma concentration was found to vary within wide
limits depending on the particular lipophilic GLP-1 derivative selected. The efficacy of several prepared derivs. was tested by stimulation of cAMP in a cell line expressing cloned human GLP-1 receptor.

ST lipophilic **glucagon** like peptide prepn antidiabetic; antiobesity agent lipophilic **glucagon** like peptide

IT Carboxylic acids, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(dicarboxylic, long-chain, **glucagon**-like peptide conjugates; preparation of lipophilic human **glucagon**-like peptide-1 derivs. with protracted action profiles)

IT Fatty acids, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**glucagon**-like peptide conjugates; preparation of lipophilic human **glucagon**-like peptide-1 derivs. with protracted action profiles)

IT Antidiabetic agents
Antiobesity agents
(preparation of lipophilic human **glucagon**-like peptide-1 derivs. with protracted action profiles)

IT Peptides, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of lipophilic human **glucagon**-like peptide-1 derivs. with protracted action profiles)

IT **240133-31-7P 240133-32-8P 240133-33-9P**
240133-35-1P 240480-97-1P 240480-98-2P **240480-99-3P**
240481-01-0P 240481-02-1P **240481-03-2P** 240481-04-3P
240481-05-4P 240481-06-5P 240481-07-6P **240481-08-7P**
240481-09-8P 240481-10-1P 240481-11-2P **240481-12-3P**
240481-13-4P 240481-22-5P 240481-24-7P
240481-25-8P 240481-27-0P 240481-32-7P
240481-33-8P 240481-35-0P 240482-41-1P 240482-42-2P
240482-43-3P 240482-44-4P 240482-45-5P 240483-55-0P 240483-71-0P
240497-59-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(**glucagon**-like peptide conjugates; preparation of lipophilic human **glucagon**-like peptide-1 derivs. with protracted action profiles)

IT 56-12-2, γ-Aminobutyric acid, reactions 107-95-9, β-Alanine
13406-98-9, 1-Piperidinecarboxylic acid 14565-47-0 22102-66-5
25456-76-2 55889-33-3 176435-11-3 240133-43-1 240133-44-2
240133-45-3 240133-46-4 240133-47-5 240133-48-6 240133-49-7
240133-50-0 240133-51-1 240481-37-2 240481-39-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(**glucagon**-like peptide conjugates; preparation of lipophilic human **glucagon**-like peptide-1 derivs. with protracted action profiles)

IT 14464-30-3P 111333-92-7P 240133-29-3P 240133-30-6P 240133-34-0P
240133-36-2P 240133-37-3P 240133-38-4P 240133-39-5P 240133-40-8P
240133-41-9P 240133-42-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(**glucagon**-like peptide conjugates; preparation of lipophilic human **glucagon**-like peptide-1 derivs. with protracted action profiles)

IT 56-81-5, Glycerol, biological studies 69-65-8, Mannitol 99-76-3, Methyl p-hydroxybenzoate 100-51-6, Benzenemethanol, biological studies 108-39-4, m-Cresol, biological studies 108-95-2, Phenol, biological studies 127-09-3, Sodium acetate 7440-66-6, Zinc, biological studies 7632-05-5, Sodium phosphate 7647-14-5, Sodium chloride, biological studies 11061-68-0, Human insulin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical composition; preparation of lipophilic human **glucagon**-like peptide-1 derivs. with protracted action profiles)

IT **106612-94-6**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); **THU (Therapeutic use)**; BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(preparation of lipophilic human **glucagon**-like peptide-1 derivs. with protracted action profiles)

IT **87805-34-3DP**, **Glucagon**-like peptide I (human), lipophilic derivs. **89750-14-1DP**, **Glucagon**-related peptide I, lipophilic derivs. 99658-04-5DP, lipophilic derivs. **104364-62-7DP**, **Glucagon**-related peptide I (guinea pig clone gpGCG-2), lipophilic derivs. 107444-51-9DP, lipophilic derivs. 121181-17-7DP, **Glucagon**-related peptide 1 (Octodon degus), lipophilic derivs. 123475-27-4DP, lipophilic derivs. **123475-28-5DP**, lipophilic derivs. 123512-62-9DP, lipophilic derivs. **157569-66-9DP**, lipophilic derivs. **157629-57-7DP**, lipophilic derivs. **204521-54-0P 204521-55-1P** 204521-56-2P **204521-57-3P 204521-58-4P** 204521-59-5P **204521-81-3DP**, lipophilic derivs. **204521-82-4DP**, lipophilic derivs. **204521-83-5DP**, lipophilic derivs. **204521-84-6DP**, lipophilic derivs. **204521-85-7DP**, lipophilic derivs. **204521-86-8DP**, lipophilic derivs. **204521-87-9DP**, lipophilic derivs. **204521-88-0DP**, lipophilic derivs. **204521-89-1DP**, lipophilic derivs. **204521-90-4DP**, lipophilic derivs. **204521-91-5DP**, lipophilic derivs. **204521-92-6DP**, lipophilic derivs. **204655-84-5DP**, lipophilic derivs. **204655-85-6DP**, lipophilic derivs. **204655-86-7DP**, lipophilic derivs. **204655-87-8P 204655-88-9P 204655-89-0DP**, lipophilic derivs. **204655-90-3DP**, lipophilic derivs. **204655-91-4DP**, lipophilic derivs. **204655-92-5DP**, lipophilic derivs. **204655-93-6DP**, lipophilic derivs. **204655-94-7P 204655-96-9P** 204655-97-0P **204655-98-1P 204655-99-2P 204656-00-8P** **204656-01-9P** 204656-02-0P **204656-03-1DP**, lipophilic derivs. **204656-04-2DP**, lipophilic derivs. **204656-05-3DP**, lipophilic derivs. **204656-06-4DP**, lipophilic derivs. **204656-07-5DP**, lipophilic derivs. **204656-08-6P** **204656-09-7P 204656-10-0P** 204656-11-1P **204656-12-2DP**, lipophilic derivs. **204656-13-3DP**, lipophilic derivs. **204656-14-4DP**, lipophilic derivs. **204656-15-5DP**, lipophilic derivs. **204656-16-6P** **204656-17-7P 204656-18-8P 204656-20-2P** **204656-21-3P 204656-22-4DP**, lipophilic derivs. **204656-24-6DP**, lipophilic derivs. **204656-25-7P** 204656-26-8P **204656-27-9P 204656-28-0P** **204656-29-1DP**, lipophilic derivs. **204656-30-4DP**, lipophilic derivs. **204656-31-5P 204656-32-6DP**, lipophilic derivs. **204656-33-7P 204656-34-8P** **204656-35-9P 204656-36-0P 204656-37-1DP**,

lipophilic derivs. **204656-38-2P 204656-39-3DP,**
lipophilic derivs. 204656-40-6P 204656-41-7P **204656-42-8DP,**
lipophilic derivs. **204656-43-9DP,** lipophilic derivs.
204656-44-0DP, lipophilic derivs. **204656-45-1DP,**
lipophilic derivs. **204656-46-2DP,** lipophilic derivs.
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lipophilic derivs. **204656-49-5DP,** lipophilic derivs.
204656-50-8DP, lipophilic derivs. **204656-51-9P**
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lipophilic derivs. **204656-74-6DP,** lipophilic derivs.
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lipophilic derivs. **204656-77-9DP,** lipophilic derivs.
204656-78-0DP, lipophilic derivs. **204656-79-1DP,**
lipophilic derivs. **204656-80-4DP,** lipophilic derivs.
204656-81-5DP, lipophilic derivs. **204656-82-6DP,**
lipophilic derivs. **204656-83-7DP,** lipophilic derivs.
204656-84-8DP, lipophilic derivs. **204656-85-9DP,**
lipophilic derivs. **204656-86-0DP,** lipophilic derivs.
204656-87-1DP, lipophilic derivs. **204656-88-2DP,**
lipophilic derivs. **204656-89-3DP,** lipophilic derivs.
204656-90-6DP, lipophilic derivs. **204656-91-7DP,**
lipophilic derivs. **204656-92-8DP,** lipophilic derivs.
204656-93-9DP, lipophilic derivs. **204656-94-0DP,**
lipophilic derivs. **204656-95-1DP,** lipophilic derivs.
204656-96-2DP, lipophilic derivs. **204656-97-3DP,**
lipophilic derivs. **204996-97-4P,** NNC 901167
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of lipophilic human **glucagon**-like peptide-1 derivs. with protracted action profiles)

IT 434-13-9, Lithocholic acid 14464-31-4 14464-32-5 45120-30-7, L-Glutamic acid α-tert-butyl ester 69888-86-4 128746-57-6
146004-82-2 146004-83-3 146004-84-4 146004-85-5 204521-68-6
204521-69-7 204521-70-0 204521-71-1 204521-72-2 204521-73-3
204521-75-5 204655-83-4 204655-95-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of lipophilic human **glucagon**-like peptide-1 derivs. with protracted action profiles)

IT 104211-94-1P 204521-61-9P 204521-63-1P 204521-65-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of lipophilic human **glucagon**-like peptide-1 derivs. with protracted action profiles)

IT 204655-84-5 204655-85-6 204655-86-7 204655-89-0 204655-90-3
204655-91-4 204655-93-6 204656-04-2 204656-05-3 204656-06-4
204656-07-5 204656-12-2 204656-13-3 204656-15-5 204656-24-6
204656-29-1 204656-32-6 204656-39-3 204656-42-8 204656-44-0
204656-46-2 204656-48-4 204656-50-8
204656-52-0 204656-53-1 204656-54-2 204656-55-3 204656-57-5

204656-62-2 204656-65-5 204656-66-6 204656-68-8 204656-69-9
204656-73-5 204656-79-1 **362514-47-4** 362514-51-0
362514-52-1 362514-59-8 362514-71-4 362514-72-5 362514-73-6
362514-74-7 362514-75-8 362514-76-9 362514-77-0 362514-78-1
362514-84-9 362514-90-7 362514-91-8 362514-92-9 362514-93-0
362514-94-1 362514-95-2 362514-96-3 **362514-97-4**
362514-98-5 362515-00-2 362515-01-3 362515-03-5 362515-04-6
362515-05-7 362517-26-8 362517-42-8 362517-44-0 362517-45-1
362517-46-2 362517-49-5 362517-51-9 **362517-52-0**
362517-61-1
RL: PRP (Properties)
(unclaimed protein sequence; preparation of lipophilic human **glucagon**-like peptide-1 derivs. with protracted action profiles)

IT 204655-92-5 204656-14-4 362014-49-1 362014-50-4 362014-51-5
RL: PRP (Properties)
(unclaimed sequence; preparation of lipophilic human **glucagon**-like peptide-1 derivs. with protracted action profiles)

RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Anon; WO 9011296 1990 HCAPLUS
(2) Anon; WO 9111457 1991 HCAPLUS
(3) Anon; WO 9507931 1995 HCAPLUS
(4) Anon; WO 9531214 1995 HCAPLUS
(5) Anon; EP 0708179 1996 HCAPLUS
(6) Anon; WO 9629342 1996 HCAPLUS
(7) Anon; WO 9629344 1996 HCAPLUS
(8) Anon; WO 8706941 1997 HCAPLUS
(9) Anon; WO 9808531 1998 HCAPLUS
(10) Anon; WO 9808871 1998 HCAPLUS
(11) Anon; WO 9808873 1998 HCAPLUS
(12) Anon; WO 9819698 1998 HCAPLUS
(13) Buckley; US 5545618 1996 HCAPLUS
(14) Chen; US 5512549 1996 HCAPLUS
(15) Clodfelter; Pharmaceutical Res 1998, V15(2), P254 HCAPLUS
(16) Habener; US 5120712 1992 HCAPLUS
(17) Habener; US 5614492 1997 HCAPLUS
(18) Kim; J of Pharma, Sciences 1994, V83(8), P1175 HCAPLUS

L58 ANSWER 4 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:598461 HCAPLUS
DN 135:200441
ED Entered STN: 17 Aug 2001
TI **Glucagon**-like peptide-1 crystals
IN Hermeling, Ronald Norbert; Hoffmann, James Arthur; Narasimhan, Chakavarthy
PA USA
SO U.S. Pat. Appl. Publ., 17 pp.
CODEN: USXXCO
DT Patent
LA English
IC ICM A61K038-00
ICS C07K017-00; C07K016-00; C07K014-00; C07K001-00; A23J001-00
NCL 514012000
CC 63-6 (**Pharmaceuticals**)
Section cross-reference(s): 2
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	US 2001014666	A1	20010816	US 1998-209799	19981211	<--
	US 6380357	B2	20020430			
	US 2003045464	A1	20030306	US 2001-997792	20011130	<--
	US 6555521	B2	20030429			
PRAI	US 1997-69728P	P	19971216	<--		

US 1998-209799 A1 19981211 <--

AB The invention provides individual tetragonal flat rod shaped or plate-like crystals of **glucagon**-like peptide-1 related mols., processes for their preparation, compns. and methods of use. The crystal prepns. exhibit extended time action in vivo and are useful for treating diabetes, obesity and related conditions.

ST **glucagon** like peptide 1 crystal antidiabetic

IT Peptides, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(GLP-1 analogs; **glucagon**-like peptide-1 crystals for preparation of extended-action pharmaceuticals)

IT Drug delivery systems
(carriers; **glucagon**-like peptide-1 crystals for preparation of extended-action pharmaceuticals)

IT Drug delivery systems
(extended-action; **glucagon**-like peptide-1 crystals for preparation of extended-action pharmaceuticals)

IT Antidiabetic agents
Antiobesity agents
Buffers
Crystal morphology
Crystallization
Protein sequences
Solvents
pH
(**glucagon**-like peptide-1 crystals for preparation of extended-action pharmaceuticals)

IT Alcohols, uses
Disaccharides
Monosaccharides
RL: NUU (Other use, unclassified); PEP (Physical, engineering or chemical process); PROC (Process); USES (Uses)
(**glucagon**-like peptide-1 crystals for preparation of extended-action pharmaceuticals)

IT 54249-88-6, dipeptidyl peptidase IV
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**glucagon**-like peptide-1 crystals for preparation of extended-action pharmaceuticals)

IT 50-69-1, Ribose 50-99-7, Glucose, uses 56-40-6, Glycine, uses 56-81-5, Glycerol, uses 56-84-8, Aspartic acid, uses 57-48-7, Fructose, uses 57-50-1, Sucrose, uses 59-23-4, Galactose, uses 63-42-3, Lactose 64-17-5, Ethanol, uses 67-56-1, Methanol, uses 69-65-8, Mannitol 69-79-4, Maltose 71-23-8, Propanol, uses **77-86-1**, Tris 99-20-7, Trehalose 127-09-3, Sodium acetate 631-61-8, Ammonium acetate 1758-51-6, Erythrose 6976-37-0, bis-tris 7440-66-6, Zinc, uses 7646-85-7, Zinc chloride, uses 7783-20-2, Ammonium sulfate, uses
RL: NUU (Other use, unclassified); PEP (Physical, engineering or chemical process); PROC (Process); USES (Uses)
(**glucagon**-like peptide-1 crystals for preparation of extended-action pharmaceuticals)

IT **89750-14-1, Glucagon**-like peptide I **106612-94-6**
123475-27-4 **123475-28-5 127650-06-0**
138347-76-9 138347-77-0 170098-75-6 **194551-05-8**
213754-29-1 213754-33-7 **227472-22-2 352513-61-2**
352513-69-0 352513-70-3 352513-71-4
352513-72-5 352513-73-6 352513-74-7
352513-75-8 352681-26-6 355393-49-6 355393-50-9
355393-52-1 355393-53-2 355470-33-6 355470-34-7 355804-31-8

355804-33-0
RL: PEP (Physical, engineering or chemical process); PRP (Properties); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(**glucagon**-like peptide-1 crystals for preparation of extended-action pharmaceuticals)

L58 ANSWER 5 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:566665 HCAPLUS
DN 135:122756
ED Entered STN: 06 Aug 2001
TI Preparation of lipophilic human **glucagon**-like peptide-1 derivatives with protracted action profiles
IN Knudsen, Liselotte Bjerre; Huusfeldt, Per Olaf; Nielsen, Per Franklin; Kaarsholm, Niels C.; Olsen, Helle Birk; Bjorn, Soren Erik; Pedersen, Freddy Zimmerdahl; Madsen, Kjeld
PA Den.
SO U.S. Pat. Appl. Publ., 133 pp., Cont.-in-part of U.S. Ser. No. 265,141.
CODEN: USXXCO
DT Patent
LA English
IC A61K038-00
NCL 514012000
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): **1**, **63**
FAN.CNT 12

	PATENT NO.	KIND	DATE		APPLICATION NO.	DATE	
PI	US 2001011071	A1	20010802		US 1999-398111	19990916	<--
	US 6458924	B2	20021001				
	WO 9808871	A1	19980305		WO 1997-DK340	19970822	<--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM						
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG						
	JP 2001011095	A2	20010116		JP 2000-152778	19970822	<--
	ZA 9707791	A	19980302		ZA 1997-7791	19970829	<--
	ZA 9707828	A	19980302		ZA 1997-7828	19970901	<--
	US 6268343	B1	20010731		US 1999-258750	19990226	<--
	US 6384016	B1	20020507		US 1999-265141	19990308	<--
	US 2002025933	A1	20020228		US 2001-908534	20010718	<--
	US 2003199672	A1	20031023		US 2002-285079	20020819	<--
PRAI	DK 1996-931	A	19960830	<--			
	DK 1996-1259	A	19961108	<--			
	DK 1996-1470	A	19961220	<--			
	US 1997-36255P	P	19970124	<--			
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	US 1998-84357P	P	19970822	<--			
	WO 1997-DK340	W	19970822	<--			
	US 1997-918810	B2	19970826	<--			
	DK 1998-263	A	19980227	<--			
	DK 1998-264	A	19980227	<--			
	DK 1998-268	A	19980227	<--			
	US 1998-38432	B2	19980311	<--			
	US 1998-78422P	P	19980318	<--			
	US 1998-82478P	P	19980421	<--			
	US 1998-82479P	P	19980421	<--			
	US 1998-82480P	P	19980421	<--			
	US 1998-82802P	P	19980423	<--			

US 1999-258750	A2	19990226	
US 1999-265141	A2	19990308	
US 1997-35904P	P	19970124	<--
US 1997-35905P	P	19970124	<--
JP 1998-511183	A3	19970822	<--
US 1997-922200	B2	19970902	<--
DK 1998-271	A	19980227	<--
DK 1998-272	A	19980227	<--
DK 1998-274	A	19980227	<--
EP 1998-610006	A	19980313	<--
DK 1998-507	A	19980408	<--
DK 1998-508	A	19980408	<--
DK 1998-509	A	19980408	<--
US 1998-85789P	P	19980518	<--
US 1999-258187	B1	19990225	
US 1999-398111	A1	19990916	

OS MARPAT 135:122756

AB The present invention relates to pharmaceutical compns. comprising lipophilic human **glucagon**-like peptide-1 (GLP-1) derivs. having a lipophilic substituent and a surfactant. Thus, coupling of GLP-1(7-37)-OH with Me(CH2)12CO-Glu(OSu)-OCMe3 (Su = succinimidyl) (preparation given), followed by deesterification with CF3CO2H and chromatog. purification gave 8% bis-adduct Lys[Me(CH2)12CO-γ-Glu]26,34-GLP-1(7-37)-OH. Several prepared lipophilic GLP-1 analogs were tested for protracted plasma concentration in pigs and were found to be much more persistent than GLP-1(7-37). In addition, the time of peak plasma concentration was found to vary within wide limits depending on the particular lipophilic GLP-1 derivative selected. The efficacy of several prepared derivs. was tested by stimulation of cAMP in a cell line expressing cloned human GLP-1 receptor.

ST lipophilic **glucagon** like peptide prepn antidiabetic; antiobesity agent lipophilic **glucagon** like peptide

IT Glycerophospholipids
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cephalins, pharmaceutical composition; preparation of lipophilic human **glucagon**-like peptide-1 derivs. with protracted action profiles)

IT Carboxylic acids, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(dicarboxylic, long-chain, **glucagon**-like peptide conjugates; preparation of lipophilic human **glucagon**-like peptide-1 derivs. with protracted action profiles)

IT Castor oil
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ethoxylated, pharmaceutical composition; preparation of lipophilic human **glucagon**-like peptide-1 derivs. with protracted action profiles)

IT Fatty acids, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**glucagon**-like peptide conjugates; preparation of lipophilic human **glucagon**-like peptide-1 derivs. with protracted action profiles)

IT Glycolipids
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(glyceroglycolipids, pharmaceutical composition; preparation of lipophilic human **glucagon**-like peptide-1 derivs. with protracted action profiles)

IT Lysophosphatides
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lysophosphatidylthreonines, pharmaceutical composition; preparation of lipophilic human **glucagon**-like peptide-1 derivs. with protracted action profiles)

IT Detergents
(pharmaceutical composition; preparation of lipophilic human **glucagon**-like peptide-1 derivs. with protracted action profiles)

IT Glycerides, biological studies
Glycosphingolipids
Lecithins
Lysophosphatidylcholines
Lysophosphatidylserines
Lysophospholipids
Phosphatidylcholines, biological studies
Phosphatidylserines
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical composition; preparation of lipophilic human **glucagon**-like peptide-1 derivs. with protracted action profiles)

IT Sphingolipids
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphosphingolipids, pharmaceutical composition; preparation of lipophilic human **glucagon**-like peptide-1 derivs. with protracted action profiles)

IT Antidiabetic agents
Antiobesity agents
(preparation of lipophilic human **glucagon**-like peptide-1 derivs. with protracted action profiles)

IT Peptides, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of lipophilic human **glucagon**-like peptide-1 derivs. with protracted action profiles)

IT **240133-31-7P 240133-32-8P 240133-33-9P**
240133-35-1P 240480-97-1P 240480-98-2P **240480-99-3P**
240481-01-0P 240481-02-1P **240481-03-2P** 240481-04-3P
240481-05-4P 240481-06-5P 240481-07-6P **240481-08-7P**
240481-09-8P 240481-10-1P 240481-11-2P **240481-12-3P**
240481-13-4P 240481-22-5P 240481-24-7P
240481-25-8P 240481-27-0P 240481-32-7P
240481-33-8P 240481-35-0P 240482-41-1P 240482-42-2P
240482-43-3P 240482-44-4P 240482-45-5P 240483-55-0P 240483-71-0P
240497-59-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(**glucagon**-like peptide conjugates; preparation of lipophilic human **glucagon**-like peptide-1 derivs. with protracted action profiles)

IT 56-12-2, γ-Aminobutyric acid, reactions 107-95-9, β-Alanine
13406-98-9, 1-Piperidinecarboxylic acid 14565-47-0 22102-66-5
25456-76-2 55889-33-3 176435-11-3 **204521-81-3**
240133-43-1 240133-44-2 240133-45-3 **240133-46-4**
240133-47-5 240133-48-6 240133-49-7 240133-50-0 240133-51-1
240481-37-2 240481-39-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(**glucagon**-like peptide conjugates; preparation of lipophilic human **glucagon**-like peptide-1 derivs. with protracted action profiles)

IT 14464-30-3P 111333-92-7P 240133-29-3P 240133-30-6P 240133-34-0P
240133-36-2P 240133-37-3P 240133-38-4P 240133-39-5P 240133-40-8P
240133-41-9P 240133-42-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(**glucagon**-like peptide conjugates; preparation of lipophilic human **glucagon**-like peptide-1 derivs. with protracted action profiles)

IT 56-81-5, Glycerol, biological studies 57-09-0, Cetyltrimethylammonium bromide 69-65-8, Mannitol 81-25-4, Cholic acid 99-76-3, Methyl p-hydroxybenzoate 100-51-6, Benzenemethanol, biological studies 108-39-4, m-Cresol, biological studies 108-95-2, Phenol, biological studies 123-03-5, Cetylpyridinium chloride 128-49-4 145-42-6, Sodium taurocholate 151-21-3, Sodium dodecyl sulfate, biological studies 300-62-9, Amphetamine 302-95-4, Sodium deoxycholate 577-11-7 863-57-0, Sodium glycocholate 1984-06-1, Sodium caprylate 2644-64-6, Dipalmitoylphosphatidylcholine 3239-44-9, Dexfenfluramine 3476-42-4 7491-09-0 7647-14-5, Sodium chloride, biological studies 9002-72-6, Growth hormone **9002-92-0**, brij-35 9002-93-1, triton x-100 9005-64-5, tween-20 9005-65-6, tween-80 9005-66-7, tween-40 9007-92-5, **Glucagon**, biological studies 11061-68-0, Human insulin 13699-45-1 19698-29-4, Dipalmitoyl phosphatidic acid 29557-51-5, Dodecylphosphocholine 42907-92-6, Sodium taurodihydrofusidate 58930-05-5 59122-55-3, Dodecyl β-D-glucopyranoside 75621-03-3 75795-82-3 96829-58-2, Orlistat 106650-56-0, Sibutramine 169494-85-3, Leptin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical composition; preparation of lipophilic human **glucagon**-like peptide-1 derivs. with protracted action profiles)

IT **204521-68-6DP**, lipophilic derivs.
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of lipophilic human **glucagon**-like peptide-1 derivs. with protracted action profiles)

IT **106612-94-6**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); **THU (Therapeutic use)**; BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(preparation of lipophilic human **glucagon**-like peptide-1 derivs. with protracted action profiles)

IT **87805-34-3DP**, **Glucagon**-like peptide I (human), lipophilic derivs. **89750-14-1DP**, **Glucagon**-related peptide I, lipophilic derivs. 99658-04-5DP, lipophilic derivs. **104364-62-7DP**, **Glucagon**-related peptide I (guinea pig clone gpGCG-2), lipophilic derivs. **106612-94-6DP**, **Glucagon**-like peptide I(7-37) (human), lipophilic derivs. 107444-51-9DP, lipophilic derivs. 121181-17-7DP, **Glucagon**-related peptide 1 (Octodon degus), lipophilic derivs. 123475-27-4DP, lipophilic derivs. **123475-28-5DP**, lipophilic derivs. 123512-62-9DP, lipophilic derivs. **157569-66-9DP**, lipophilic derivs. **157629-57-7DP**, lipophilic derivs. **204521-54-0P** **204521-55-1P** 204521-56-2P **204521-57-3P** **204521-58-4P** 204521-59-5P **204521-69-7DP**, lipophilic derivs. **204521-70-0DP**, lipophilic derivs. **204521-72-2DP**, lipophilic derivs. **204521-81-3DP**, lipophilic derivs. **204521-82-4DP**, lipophilic derivs. **204521-83-5DP**, lipophilic derivs. **204521-84-6DP**, lipophilic derivs. **204521-85-7DP**, lipophilic derivs. **204521-86-8DP**, lipophilic derivs. **204521-87-9DP**, lipophilic derivs. **204521-88-0DP**, lipophilic derivs. **204521-89-1DP**, lipophilic derivs. **204521-90-4DP**, lipophilic derivs. **204521-91-5DP**, lipophilic derivs. **204521-92-6DP**, lipophilic derivs. **204655-84-5DP**, lipophilic derivs. **204655-85-6DP**, lipophilic derivs. **204655-86-7DP**,

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204655-89-0DP, lipophilic derivs. **204655-90-3DP**,
lipophilic derivs. **204655-91-4DP**, lipophilic derivs.
204655-92-5DP, lipophilic derivs. **204655-93-6DP**,
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lipophilic derivs. **204656-96-2DP**, lipophilic derivs.
204656-97-3DP, lipophilic derivs. **204996-97-4P**, NNC
901167
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of lipophilic human **glucagon**-like peptide-1 derivs. with protracted action profiles)

IT 434-13-9, Lithocholic acid 14464-31-4 14464-32-5 45120-30-7, L-Glutamic acid α-tert-butyl ester 69888-86-4 128746-57-6 146004-82-2 146004-83-3 146004-84-4 146004-85-5 **204521-68-6** **204521-69-7** **204521-70-0** 204521-71-1 **204521-72-2** 204521-73-3 204521-75-5 204655-83-4 204655-95-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of lipophilic human **glucagon**-like peptide-1 derivs. with protracted action profiles)

IT 104211-94-1P 204521-61-9P 204521-63-1P 204521-65-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of lipophilic human **glucagon**-like peptide-1 derivs. with protracted action profiles)

L58 ANSWER 6 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:441646 HCAPLUS
DN 133:64006
ED Entered STN: 30 Jun 2000
TI Shelf-stable formulation of **glucagon**-like peptide-1
IN **Brader, Mark L.; Pekar, Allen H.**
PA Eli Lilly and Company, USA
SO PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K038-26
ICS A61K038-28; A61K047-10; A61K047-26; A61P003-10; A61K038-28; A61K038-26
CC 63-6 (**Pharmaceuticals**)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000037098	A1	20000629	WO 1999-US30395	19991221 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2358107	AA	20000629	CA 1999-2358107	19991221 <--
EP 1140148	A1	20011010	EP 1999-967463	19991221 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002532557	T2	20021002	JP 2000-589208	19991221 <--
PRAI US 1998-113499P	P	19981222 <--		
WO 1999-US30395	W	19991221		

AB **Glucagon**-like peptide-1 (GLP-1) has been shown to be useful in the treatment of diabetes. The invention encompasses a shelf-stable formulation that comprises a therapeutically effective amount of GLP-1, a pharmaceutically acceptable preservative, and a tonicity modifier, and that has a pH between about 8.2 to about 8.8. Val(8) GLP-1 (66.2 mg) was dissolved in water at 1.0 mg/mL and adjusted to pH 8.51. A 21.5 mL aliquot of peptide solution in water was mixed with 21.5 mL of 0.63% m-cresol-3.2% glycerol-0.02M pH 8.5 Tris buffer and the final pH was set to 8.50. Aliquots of the solution, containing 0.5 mg/mL peptide in 0.315%

m-cresol-1.6% glycerol- 0.01M Tris at pH 8.50, were pipetted into parenteral vials. GLP-1 in Tris buffer had the highest purity, and hence the highest stability values.

ST shelf life stability formulation **glucagon** peptide; **glucagon** like peptide shelf life stability

IT Drug delivery systems
(parenterals; shelf-stable formulation of **glucagon**-like peptide-1)

IT Buffers
Drug delivery systems
Surfactants
(shelf-stable formulation of **glucagon**-like peptide-1)

IT 56-87-1, Lysine, biological studies **77-86-1**, Tris
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(shelf-stable formulation of **glucagon**-like peptide-1)

IT **89750-14-1**, **Glucagon**-like peptide I **123475-28-5** **127650-06-0** **194551-05-8**
RL: PRP (Properties); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(shelf-stable formulation of **glucagon**-like peptide-1)

IT **9002-92-0**, Brij-35
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(shelf-stable formulation of **glucagon**-like peptide-1)

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Gen Hospital Corp; WO 8706941 A 1987 HCAPLUS
(2) Habener, J; US 5118666 A 1992 HCAPLUS
(3) Lilly Co Eli; EP 0733644 A 1996 HCAPLUS
(4) London Health Ass; WO 9531214 A 1995 HCAPLUS
(5) Novonordisk As; WO 9620005 A 1996 HCAPLUS

L58 ANSWER 7 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:161155 HCAPLUS
DN 132:212699
ED Entered STN: 10 Mar 2000
TI Method for administering insulinotropic peptides
IN Hughes, Benjamin Lee; Wolff, Ronald Keith
PA Eli Lilly and Company, USA
SO PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K038-16
CC 63-6 (**Pharmaceuticals**)
Section cross-reference(s): **1**, 2

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 2000012116	A1	20000309	WO 1999-US19348	19990824	<--
	W: AE, AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CR, CU, CZ, DM, EE, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
	CA 2341454	AA	20000309	CA 1999-2341454	19990824	<--
	AU 9955841	A1	20000321	AU 1999-55841	19990824	<--
	AU 764371	B2	20030814			
	BR 9913284	A	20010515	BR 1999-13284	19990824	<--
	JP 2002523466	T2	20020730	JP 2000-567230	19990824	<--
	EP 997151	A2	20000503	EP 1999-306733	19990825	<--

EP 997151 A3 20000920
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
ZA 2001001541 A 20020523 ZA 2001-1541 20010223 <--
NO 2001000982 A 20010427 NO 2001-982 20010227 <--
HR 2001000141 A1 20020228 HR 2001-141 20010227 <--
PRAI US 1998-98273P P 19980828 <--
US 1998-100012P P 19980911 <--
WO 1999-US19348 W 19990824

AB The claimed invention relates to a method of administering **glucagon**-like peptide-1 mols. by inhalation, a method for treating diabetes by administering **glucagon**-like peptide-1 mols. by inhalation, and a method for treating hyperglycemia by administering **glucagon**-like peptide-1 mols. by inhalation. There was good bioavailability of Val8-GLP-1 delivered to the lungs of dogs by inhalation relative to s.c. administration.

ST **glucagon** like peptide inhalation; antidiabetic insulinotropic peptide inhalation

IT Drug delivery systems
(inhalants; inhalation administration of insulinotropic peptides)

IT Antidiabetic agents
(inhalation administration of insulinotropic peptides)

IT Drug delivery systems
(sprays; inhalation administration of insulinotropic peptides)

IT **194551-05-8**, Val8-GLP-1
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(inhalation administration of insulinotropic peptides)

IT **89750-14-1, Glucagon**-like peptide I **89750-14-1D**
, **Glucagon**-like peptide I, derivs.
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhalation administration of insulinotropic peptides)

IT 260551-81-3 260551-82-4 260551-84-6
RL: PRP (Properties)
(unclaimed protein sequence; method for administering insulinotropic peptides)

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Buckley; US 5545618 A 1996 HCAPLUS
(2) Chen; US 5512549 A 1996 HCAPLUS

L58 ANSWER 8 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:133809 HCAPLUS
DN 132:175839
ED Entered STN: 25 Feb 2000
TI Differentiation of non-insulin producing cells into insulin producing cells by GLP-1 or Exendin-4 and uses thereof
IN Egan, Josephine; Perfetti, Riccardo; Passaniti, Antonino; Greig, Nigel; Holloway, Harold
PA United States of America, Department of Health and Human Services, USA
SO PCT Int. Appl., 119 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12N005-06
ICS A61K038-22; A61K038-26; C07K014-605; C07K014-575
CC 1-10 (**Pharmacology**)
Section cross-reference(s): **63**

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000009666	A2	20000224	WO 1999-US18099	19990810 <--

WO 2000009666 A3 20001123
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
CA 2339326 AA 20000224 CA 1999-2339326 19990810 <--
AU 9955524 A1 20000306 AU 1999-55524 19990810 <--
EP 1105460 A2 20010613 EP 1999-942066 19990810 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
PRAI US 1998-95917P P 19980810 <--
WO 1999-US18099 W 19990810

AB The present invention relates to a population of insulin producing cells made by a process comprising contacting non-insulin producing cells with a growth factor selected from the group consisting of GLP-1 or Exendin-4, growth factors having amino acid sequences substantially homologous to GLP-1 or Exendin-4, and fragments thereof. The present invention also relates to methods of differentiating non-insulin producing cells into insulin producing cells and of enriching a population of cells for insulin-producing cells. The present invention also relates to methods of treating diabetes. Exendin-4 was more potent an insulinotropic agent than GLP-1 on several levels when given i.v.

ST insulin cell differentiation growth factor; **glucagon** like peptide 1 insulin cell differentiation; Exendin 4 insulin cell differentiation; diabetes treatment cell differentiation insulin

IT Animal cell line
(AR42J; differentiation of non-insulin producing cells into insulin producing cells by GLP-1 or Exendin-4 and uses thereof)

IT Pancreas
(acinar cell; differentiation of non-insulin producing cells into insulin producing cells by GLP-1 or Exendin-4 and uses thereof)

IT Pancreas
(cell of; differentiation of non-insulin producing cells into insulin producing cells by GLP-1 or Exendin-4 and uses thereof)

IT Cell
Cell differentiation
(differentiation of non-insulin producing cells into insulin producing cells by GLP-1 or Exendin-4 and uses thereof)

IT **Glucagon**-like peptide-1 receptors
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(differentiation of non-insulin producing cells into insulin producing cells by GLP-1 or Exendin-4 and uses thereof)

IT mRNA
RL: BOC (Biological occurrence); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
(for insulin; differentiation of non-insulin producing cells into insulin producing cells by GLP-1 or Exendin-4 and uses thereof)

IT Diabetes mellitus
(insulin-dependent, treatment of; differentiation of non-insulin producing cells into insulin producing cells by GLP-1 or Exendin-4 and uses thereof)

IT Animal cell
(mammalian; differentiation of non-insulin producing cells into insulin producing cells by GLP-1 or Exendin-4 and uses thereof)

IT Cell

(stem; differentiation of non-insulin producing cells into insulin producing cells by GLP-1 or Exendin-4 and uses thereof)

IT Antigens
RL: PEP (Physical, engineering or chemical process); PROC (Process)
(surface, alteration of, on cell surface; differentiation of non-insulin producing cells into insulin producing cells by GLP-1 or Exendin-4 and uses thereof)

IT Diabetes mellitus
(treatment of; differentiation of non-insulin producing cells into insulin producing cells by GLP-1 or Exendin-4 and uses thereof)

IT 9004-10-8P, Insulin, biological studies
RL: BOC (Biological occurrence); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
(differentiation of non-insulin producing cells into insulin producing cells by GLP-1 or Exendin-4 and uses thereof)

IT 9007-92-5, **Glucagon**, biological studies
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(differentiation of non-insulin producing cells into insulin producing cells by GLP-1 or Exendin-4 and uses thereof)

IT **89750-14-1**, **Glucagon**-like peptide I **89750-14-1D**
, **Glucagon**-like peptide I, homologs or fragments 141732-76-5, Exendin-4 141732-76-5D, Exendin-4, homologs or fragments
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(differentiation of non-insulin producing cells into insulin producing cells by GLP-1 or Exendin-4 and uses thereof)

IT 7440-70-2, Calcium, biological studies
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(intracellular, GLP-1 effect on; differentiation of non-insulin producing cells into insulin producing cells by GLP-1 or Exendin-4 and uses thereof)

IT 9000-92-4P, Amylase
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(pancreatic cells producing; differentiation of non-insulin producing cells into insulin producing cells by GLP-1 or Exendin-4 and uses thereof)

IT 259127-56-5, 8: PN: WO0009666 SEQID: 19 unclaimed DNA 259127-57-6, 9: PN: WO0009666 SEQID: 20 unclaimed DNA 259127-58-7 259127-59-8 259127-60-1 259127-61-2 259127-62-3 259127-65-6, 19: PN: WO0009666 PAGE: 58 unclaimed DNA 259127-66-7, 20: PN: WO0009666 PAGE: 58 unclaimed DNA
RL: PRP (Properties)
(unclaimed nucleotide sequence; differentiation of non-insulin producing cells into insulin producing cells by GLP-1 or Exendin-4 and uses thereof)

IT 203743-40-2 238411-01-3 238411-05-7 238411-07-9 238411-10-4 238748-48-6 259127-63-4, 15: PN: WO0009666 PAGE: 46 unclaimed DNA 259127-64-5, 16: PN: WO0009666 PAGE: 46 unclaimed DNA 259141-41-8
RL: PRP (Properties)
(unclaimed protein sequence; differentiation of non-insulin producing cells into insulin producing cells by GLP-1 or Exendin-4 and uses thereof)

IT 106612-94-6 123475-27-4 **123475-28-5** 123475-29-6 **127650-06-0** 165338-05-6, 1-31-Exendin 4 (Heloderma suspectum) 210712-28-0, 1-30-Exendin 4 (Heloderma suspectum) 216172-92-8, 7-30-**Glucagon**-like peptide 1 (Octodon degus) 238091-78-6 259088-25-0 259088-26-1
RL: PRP (Properties)
(unclaimed sequence; differentiation of non-insulin producing cells

into insulin producing cells by GLP-1 or Exendin-4 and uses thereof)

L58 ANSWER 9 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:116918 HCAPLUS
DN 132:147179
ED Entered STN: 18 Feb 2000
TI Use of GLP-1 and analogues for preventing type II diabetes
IN Nielsen, Jens Hoiriis; Friedrichsen, Birgitte Nissen; Rugh, Susanne; Tromholt, Niels; Bjorn, Soren; Knudsen, Liselotte Bjerre; Sturis, Jeppe
PA Novo Nordisk A/s, Den.
SO PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K038-26
ICS A61P003-10
CC 2-6 (Mammalian Hormones)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000007617	A1	20000217	WO 1999-DK424	19990729 <--
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9950272	A1	20000228	AU 1999-50272	19990729 <--
	EP 1100530	A1	20010523	EP 1999-934520	19990729 <--
	EP 1100530	B1	20031008		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	EP 1306091	A2	20030502	EP 2002-26139	19990729 <--
	EP 1306091	A3	20030521		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
	AT 251465	E	20031015	AT 1999-934520	19990729 <--
	US 2003224983	A1	20031204	US 2002-191351	20020703 <--
PRAI	DK 1998-998	A	19980731 <--		
	DK 1998-1025	A	19980812 <--		
	US 1998-96117P	P	19980810 <--		
	US 1998-97604P	P	19980824 <--		
	EP 1999-934520	A3	19990729		
	WO 1999-DK424	W	19990729		
	US 1999-364410	B1	19990730		
	US 2000-678683	A1	20001003		

AB The present invention relates to a method for increasing the number and/or the size of beta cells, for stimulating beta cell proliferation and for preventing diabetes. The invention is based on the recognition that GLP-1 acts as a beta cell growth factor. The invention also relates to a method for preventing or curing Type I or Type II diabetes, a method for obtaining a less severe disease stage in a subject suffering from Type II diabetes as well as methods of delaying the progression of impaired glucose tolerance (IGT) or non-insulin requiring Type II diabetes to insulin requiring Type II diabetes. The invention also relates to a cure for diabetes.
ST GLP1 analog type II diabetes prevention
IT Diabetes mellitus
(insulin-dependent; use of GLP-1 and analogs for preventing type II diabetes)

IT Diabetes mellitus
(non-insulin-dependent; use of GLP-1 and analogs for preventing type II diabetes)
IT Antidiabetic agents
(use of GLP-1 and analogs for preventing type II diabetes)
IT **89750-14-1**, **Glucagon**-like peptide I **89750-14-1D**
, **Glucagon**-like peptide I, analogs and agonists
106612-94-6, Human **glucagon**-like peptide 1 (7-37)
107444-51-9, Human **glucagon**-like peptide-1 (7-36)amide
194551-05-8 **204656-20-2** 213754-29-1 213754-31-5
213754-33-7 213754-35-9 224638-84-0 **227472-22-2**
258289-68-8
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(use of GLP-1 and analogs for preventing type II diabetes)
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Byrne, M; Diabetic Medicine 1996, V13, P854 MEDLINE
(2) Holst, J; Diabetes 1998, V47, P1663 HCAPLUS
(3) Novo Nordisk AS; WO 9808871 A1 1998 HCAPLUS

L58 ANSWER 10 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:404857 HCAPLUS
DN 131:49498
ED Entered STN: 01 Jul 1999
TI **Glucagon**-like peptide-1 crystals
IN Hoffmann, James Arthur; Hermeling, Ronald Norbert; Narasimhan, Chakravarthy
PA Eli Lilly and Company, USA
SO PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K038-26
ICS C07K014-605
CC 63-6 (**Pharmaceuticals**)
Section cross-reference(s): 2
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9930731	A1	19990624	WO 1998-US26480	19981214	<--
	W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
	CA 2315243	AA	19990624	CA 1998-2315243	19981214	<--
	EP 926159	A2	19990630	EP 1998-310245	19981214	<--
	EP 926159	A3	20031126			
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
	AU 9918218	A1	19990705	AU 1999-18218	19981214	<--
	ZA 9811466	A	20000614	ZA 1998-11466	19981214	<--
	BR 9813658	A	20001010	BR 1998-13658	19981214	<--
	JP 2002508332	T2	20020319	JP 2000-538710	19981214	<--
	NZ 505182	A	20020531	NZ 1998-505182	19981214	<--
	NO 2000003081	A	20000808	NO 2000-3081	20000615	<--
	HR 2000000409	A1	20001031	HR 2000-409	20000616	<--
PRAI	US 1997-69728P	P	19971216	<--		
	WO 1998-US26480	W	19981214	<--		

AB The invention provides individual tetragonal flat rod shaped or plate-like crystals of **glucagon**-like peptide-1 related mols., processes for their preparation, compns. and methods of use. The crystal prepns. exhibit extended time action in vivo and are useful for treating diabetes, obesity, and related conditions.

ST **glucagon** like peptide 1 crystal antidiabetic antiobesity sequence

IT Antidiabetic agents
Antiobesity agents
Buffers
Crystallization
Protein sequences
(**glucagon**-like peptide-1 crystals for extended action in treating diabetes and obesity)

IT Alcohols, uses
Disaccharides
Monosaccharides
RL: NUU (Other use, unclassified); USES (Uses)
(**glucagon**-like peptide-1 crystals for extended action in treating diabetes and obesity)

IT Crystal morphology
(tetragonal; **glucagon**-like peptide-1 crystals for extended action in treating diabetes and obesity)

IT 54249-88-6, Dipeptidyl peptidase iv
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(-protected GLP-1; **glucagon**-like peptide-1 crystals for extended action in treating diabetes and obesity)

IT 56-40-6, Glycine, uses 56-84-8, Aspartic acid, uses 127-09-3, Sodium acetate 631-61-8, Ammonium acetate 6976-37-0, Bis-Tris
RL: NUU (Other use, unclassified); USES (Uses)
(buffer; **glucagon**-like peptide-1 crystals for extended action in treating diabetes and obesity)

IT **106612-94-6P 194551-05-8P** 213754-29-1P 213754-33-7P **227472-22-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PNU (Preparation, unclassified); PRP (Properties); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(**glucagon**-like peptide-1 crystals for extended action in treating diabetes and obesity)

IT **89750-14-1, Glucagon**-like peptide I
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**glucagon**-like peptide-1 crystals for extended action in treating diabetes and obesity)

IT 50-69-1, Ribose 50-99-7, Glucose, uses 56-81-5, Glycerol, uses 57-48-7, Fructose, uses 57-50-1, Sucrose, uses 59-23-4, Galactose, uses 63-42-3, Lactose 64-17-5, Ethanol, uses 67-56-1, Methanol, uses 69-65-8, Mannitol 69-79-4, Maltose 71-23-8, Propanol, uses **77-86-1**, Tris buffer 99-20-7, Trehalose 1758-51-6, Erythrose 7440-66-6, Zinc, uses 7646-85-7, Zinc chloride, uses 7783-20-2, Ammonium sulfate, uses
RL: NUU (Other use, unclassified); USES (Uses)
(**glucagon**-like peptide-1 crystals for extended action in treating diabetes and obesity)

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Eli Lilly and Company; EP 0658568 A1 1995 HCAPLUS
(2) Eli Lilly and Company; EP 0869135 A1 1998 HCAPLUS
(3) Pfizer Inc; EP 0619322 A2 1994 HCAPLUS

(4) Pridal; 1996, V136(1-2), P53

L58 ANSWER 11 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:390390 HCAPLUS
DN 131:49468
ED Entered STN: 24 Jun 1999
TI Oral GLP-1 formulations for antidiabetic and other therapeutic applications
IN Hoffmann, James Arthur
PA Eli Lilly and Company, USA
SO PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K038-26
CC 63-6 (Pharmaceuticals)
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9929336	A1	19990617	WO 1998-US25515	19981202	<--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
	CA 2312190	AA	19990617	CA 1998-2312190	19981202	<--
	AU 9916173	A1	19990628	AU 1999-16173	19981202	<--
	EP 1049486	A1	20001108	EP 1998-960617	19981202	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI					
	JP 2001525371	T2	20011211	JP 2000-524005	19981202	<--
	US 6358924	B1	20020319	US 2000-585181	20000601	<--
	US 2002123466	A1	20020905	US 2002-72540	20020208	<--
PRAI	US 1997-67600P	P	19971205	<--		
	WO 1998-US25515	W	19981202	<--		
	US 2000-573809	A1	20000518			

AB Methods and formulations are presented that provide for (a) the oral absorption of GLP-1 peptides that bind surfactants; and (b) long-term storage of formulations containing these peptides. For example, a GLP-1/DSS complex is administered orally instead of parenterally, which is much more convenient for, and facilitates compliance with diabetic patients and persons with other GLP-1 treated conditions.
ST GLP1 oral formulation antidiabetic sequence; glucose lowering peptide 1 oral formulation antidiabetic
IT Cytoprotective agents
(cardioprotective; oral GLP-1 formulations for antidiabetic and other therapeutic applications)
IT Metabolism, animal
(disorder, catabolic; oral GLP-1 formulations for antidiabetic and other therapeutic applications)
IT Gene, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(glp-1, peptide product; oral GLP-1 formulations for antidiabetic and other therapeutic applications)
IT Peptides, biological studies
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(glucose-lowering peptide 1; oral GLP-1 formulations for antidiabetic and other therapeutic applications)

IT Heart, disease
(infarction; oral GLP-1 formulations for antidiabetic and other therapeutic applications)
IT Antidiabetic agents
Antiobesity agents
Preservatives
Protein sequences
Surfactants
(oral GLP-1 formulations for antidiabetic and other therapeutic applications)
IT Drug delivery systems
(oral; oral GLP-1 formulations for antidiabetic and other therapeutic applications)
IT Brain, disease
(stroke; oral GLP-1 formulations for antidiabetic and other therapeutic applications)
IT **106612-94-6** 107444-51-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(amino acid sequence; oral GLP-1 formulations for antidiabetic and other therapeutic applications)
IT 56-81-5, 1,2,3-Propanetriol, biological studies 99-76-3, Methylparaben 100-51-6, Benzyl alcohol, biological studies 123-03-5, Cetylpyridinium chloride 128-49-4, Docusate calcium 145-42-6, Sodium taurocholate 151-21-3, Sodium dodecyl sulfate, biological studies 302-95-4, Sodium deoxycholate 361-09-1, Sodium cholate 577-11-7 863-57-0, Sodium glycocholate 1984-06-1, Sodium caprylate 7491-09-0, Docusate potassium 7647-14-5, Sodium chloride, biological studies **9002-92-0**, Brij 35 9002-93-1, Triton X-100 9005-65-6, Tween 80 9005-66-7, Tween 40 29777-99-9D, N-alkyl derivs. 59122-55-3, Dodecyl β-D-glucopyranoside 75621-03-3
RL: MOA (Modifier or additive use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(oral GLP-1 formulations for antidiabetic and other therapeutic applications)
IT 108-39-4, biological studies 108-95-2, Phenol, biological studies
RL: MOA (Modifier or additive use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(preservative; oral GLP-1 formulations for antidiabetic and other therapeutic applications)
RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Buckley; US 5545618 A 1996 HCAPLUS
(2) Friend; US 5811388 A 1998 HCAPLUS
(3) Habener; US 5120712 A 1992 HCAPLUS
(4) Heiber; US 5766620 A 1998 HCAPLUS
(5) Novo Nordisk AS; WO 9318785 A1 1993 HCAPLUS
(6) Novo Nordisk AS; WO 9731943 A1 1997 HCAPLUS
(7) Sawai; US 5376637 A 1994 HCAPLUS

L58 ANSWER 12 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:216939 HCAPLUS
DN 130:247048
ED Entered STN: 07 Apr 1999
TI Composition for treating diabetes mellitus and obesity
IN Forssmann, Wolf Georg; Richter, Rudolf; Adermann, Knut; Meyer, Markus
PA Germany
SO PCT Int. Appl., 38 pp.
CODEN: PIXXD2

DT Patent
LA German
IC ICM C07K014-605
ICS A61K038-22
CC 1-10 (**Pharmacology**)
Section cross-reference(s): 2
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9914239	A1	19990325	WO 1998-EP5804	19980911	<--
	W: JP, US					
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
	DE 19810515	A1	19991007	DE 1998-19810515	19980311	<--
	EP 1012188	A1	20000628	EP 1998-950026	19980911	<--
	R: AT, BE, CH, DE, ES, FR, GB, IT, LI, NL					
	JP 2001516765	T2	20011002	JP 2000-511787	19980911	<--
PRAI	DE 1997-19740081	A	19970912	<--		
	DE 1997-19757739	A	19971223	<--		
	DE 1998-19810515	A	19980311	<--		
	WO 1998-EP5804	W	19980911	<--		

AB A combination of ≥2 of (a) ≥1 hormone which stimulates cAMP production, (b) ≥1 substance which inhibits the breakdown of a cyclic nucleotide, and (c) ≥1 hormone which stimulates cGMP production is superior to any of these substances alone in stimulating insulin secretion and decreasing the blood glucose level. Component (a) is an analog or deriv. of **glucagon**-like peptide 1, (b) is a phosphodiesterase inhibitor, and (c) is a guanylate cyclase C-activating peptide, esp. a guanylin or uroguanylin fragment. These may be combined with addnl. peptide hormones which affect islet cell secretion (no data).

ST antidiabetic peptide cAMP cGMP formation; obesity treatment **glucagon** like peptide; phosphodiesterase inhibitor diabetes obesity treatment; guanylin diabetes obesity treatment; uroguanylin diabetes obesity treatment

IT Pancreas, disease
(chronic pancreatitis, secondary hyperglycemia in, treatment of; peptide composition for treating diabetes mellitus and obesity)

IT Nucleotides, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(cyclic; peptide composition for treating diabetes mellitus and obesity)

IT Lipoproteins
(dyslipoproteinemia, treatment of; peptide composition for treating diabetes mellitus and obesity)

IT Lipoproteins
(hyperlipoproteinemia, treatment of; peptide composition for treating diabetes mellitus and obesity)

IT Muscle, disease
(hypotonia, treatment of; peptide composition for treating diabetes mellitus and obesity)

IT Antidiabetic agents
Antiobesity agents
(peptide composition for treating diabetes mellitus and obesity)

IT Acromegaly
Cushing's syndrome
Hemochromatosis
Hyperthyroidism
Pheochromocytoma
(secondary hyperglycemia in, treatment of; peptide composition for treating diabetes mellitus and obesity)

IT Drug interactions
(synergistic; peptide composition for treating diabetes mellitus and

obesity)
IT 9054-75-5, Guanylate cyclase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(C; -activating peptides, for treating diabetes mellitus and obesity)
IT 9025-82-5, Phosphodiesterase 9036-21-9, Phosphodiesterase III
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; peptide composition for treating diabetes mellitus and obesity)
IT 58-55-9, Theophylline, biological studies 58-74-2, Papaverine
1393-25-5D, Secretin, analogs and derivs. 9007-92-5D, **Glucagon**
, analogs and derivs., biological studies 27277-00-5, ICI 63197
28822-58-4, IBMX 29925-17-5, Ro 20-1724 37221-79-7D, Vasoactive
intestinal peptide, analogs and derivs. 41078-02-8, Enprofylline
51022-77-6, Etazolate 57076-71-8, Denbufylline 59392-49-3D, Gastric
inhibitory peptide, analogs and derivs. 61413-54-5, Rolipram
68550-75-4, Cilostamide 70018-51-8, Quazinone 70386-06-0, Y-590
71567-77-6D, Glicentin, analogs and derivs. 73384-60-8, Sulmazole
73963-72-1, Cilostazol 74150-27-9, Pimobendan 77671-31-9, Enoximone
78415-72-2, Milrinone 83652-28-2D, Calcitonin gene-related peptide,
analogs and derivs. 84243-58-3, Imazodan 84490-12-0, Piroximone
87164-90-7, ICI 153110 89541-55-9, SKF 94120 **89750-14-1**,
Glucagon-like peptide I 89750-15-2D, **Glucagon**-like
peptide 2, analogs and derivs. 90697-57-7, Motapizone 93851-00-4, ICI
118233 94192-59-3, Lixazinone 98326-33-1, MCI-154 100510-33-6,
Adibendan 100643-96-7, Indolidan 101041-95-6, Org 30029 101975-10-4,
Zardaverine 102669-89-6, Saterinone 106602-62-4D, Amylin, analogs and
derivs. **106612-94-6** 107444-51-9, 7-36-**Glucagon**-like
peptide 1 amide 108381-22-2, UD-CG 212 112018-01-6, Bemoradan
115344-47-3, Siguazodan **119637-73-9** 120223-30-5, EMD 54622
123475-27-4 **123475-28-5 127650-06-0** 137061-48-4D,
Pituitary adenylate cyclase-activating peptide, analogs and derivs.
138324-89-7 138324-90-0 **138324-91-1** 138324-92-2
138324-93-3 138324-94-4 138324-95-5
138324-96-6 138324-97-7 138324-98-8
138324-99-9 138325-00-5 **138347-75-8 138347-76-9**
139308-65-9, Tolafentrine 144035-83-6, RP 73401 144940-98-7D,
Guanylin, peptides of 145319-90-0D, Guanylin (human reduced), peptides
of 154721-84-3 154835-90-2D, Adrenomedullin, analogs and derivs.
158078-88-7 164252-35-1D, Uroguanylin, peptides of 187224-24-4D,
peptides of 221460-16-8 221460-17-9 221460-18-0 221460-19-1
221460-20-4 221460-21-5 221460-22-6 221460-23-7 221460-24-8
221460-25-9 221460-26-0 221460-27-1 221460-28-2 221460-29-3
221460-30-6 221460-31-7 221460-32-8 221460-33-9 221460-34-0
221460-35-1 221460-36-2 221460-37-3 **221460-38-4**
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221460-49-7 **221460-50-0 221460-51-1** 221460-52-2
221460-53-3 221460-55-5 221460-57-7 221460-59-9 221460-61-3
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221460-67-9 221460-68-0 221460-69-1 221460-70-4 221460-71-5
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221460-77-1 221460-78-2 221460-79-3 221460-80-6 221460-81-7
221460-82-8 221460-83-9 221460-86-2 221460-88-4 221460-90-8
221460-92-0 221460-94-2 221460-96-4 221460-98-6 221461-00-3
221461-02-5 221461-04-7 221461-07-0 221461-09-2 221461-11-6
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); **THU (Therapeutic use)**; BIOL (Biological
study); USES (Uses)
(peptide composition for treating diabetes mellitus and obesity)
IT 60-92-4, CAMP 7665-99-8, CGMP
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM
(Metabolic formation); BIOL (Biological study); FORM (Formation,
nonpreparative); PROC (Process)
(peptide composition for treating diabetes mellitus and obesity)

RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Buckley, D; WO 9111457 A 1991 HCAPLUS
(2) Byk Gulden Lomberg Chem Fab; WO 9837894 A 1998 HCAPLUS
(3) Celltech Therapeutics Ltd; WO 9723461 A 1997 HCAPLUS
(4) Dundore; DRUG DEVELOPMENT RESEARCH 1991, V23(2), P171 HCAPLUS
(5) Fisch; EUROPEAN JOURNAL OF PHARMACOLOGY MOLECULAR PHARMACOLOGY SECTION 1995, V289(3) HCAPLUS
(6) London Health Ass; WO 9531214 A 1995 HCAPLUS
(7) Monsanto Co; US 5140102 A 1992 HCAPLUS
(8) Novonordisk As; WO 9318786 A 1993 HCAPLUS
(9) Novonordisk As; WO 9731943 A 1997 HCAPLUS
(10) Schmidtler; AMERICAN JOURNAL OF PHYSIOLOGY 1991, V260(6) HCAPLUS
(11) Takahiro, H; WO 9724334 A 1997 HCAPLUS

L58 ANSWER 13 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:338142 HCAPLUS
DN 129:23726
ED Entered STN: 05 Jun 1998
TI Use of GLP-1 peptides for suppression of appetite or induction of satiety
IN Knudsen, Liselotte Bjerre; Thim, Lars; Judge, Martin Edward; Holst, Jens Juul; Astrup, Arne Vernon; Wulff, Brigitte Schjellerup
PA Novo Nordisk A/S, Den.; Knudsen, Liselotte Bjerre; Thim, Lars; Judge, Martin Edward; Holst, Jens Juul; Astrup, Arne Vernon; Wulff, Brigitte Schjellerup
SO PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K038-26
CC 2-6 (Mammalian Hormones)
Section cross-reference(s): 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9820895	A1	19980522	WO 1997-DK509	19971107 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9748637	A1	19980603	AU 1997-48637	19971107 <--
	EP 941114	A1	19990915	EP 1997-911155	19971107 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
	JP 2001504105	T2	20010327	JP 1998-522061	19971107 <--
	ZA 9710182	A	19980512	ZA 1997-10182	19971112 <--
	US 2003232754	A1	20031218	US 2003-382438	20030306 <--
PRAI	DK 1996-1270	A	19961112 <--		
	US 1997-37661P	P	19970124 <--		
	US 1997-965135	B1	19971106 <--		
	WO 1997-DK509	W	19971107 <--		
	US 2000-723551	B1	20001128		

AB GLP-1(1-45) or a fragment or an analog thereof can be used in the preparation of a therapeutic agent for peripheral administration in the suppression of appetite or induction of satiety. Pharmaceutical formulations containing the GLP-1 peptides are also claimed.
ST GLP1 peptides appetite suppression satiety
IT Neoplasm
(isolation and purification of GLP1 peptides from anorectic tumors; use of

GLP-1 peptides for suppression of appetite or induction of satiety)
IT Appetite
(satiety; use of GLP-1 peptides for suppression of appetite or induction of satiety)
IT Antiobesity agents
Appetite depressants
(use of GLP-1 peptides for suppression of appetite or induction of satiety)
IT Drug delivery systems
(use of formulations containing GLP-1 peptides for suppression of appetite or induction of satiety)
IT 87805-34-3P, **Glucagon**-like peptide I (human) 99658-04-5P
104364-62-7P, **Glucagon**-like peptide I (guinea pig clone gpGCG-2) **106612-94-6P** 107444-51-9P **119637-73-9P**
120500-32-5P 121181-17-7P, **Glucagon**-like peptide 1 (Octodon degus) 123475-27-4P **123475-28-5P** 123512-62-9P
127650-06-0P 138324-89-7P 138324-90-0P **157507-31-8P**
157569-66-9P **157629-57-7P** **157629-58-8P**
163912-67-2P **204656-63-3P** **204656-67-7P** 207748-60-5P
207748-61-6P **207748-62-7P** **207748-63-8P**
207748-64-9P **207748-68-3P** **207868-84-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PUR (Purification or recovery); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(use of GLP-1 peptides for suppression of appetite or induction of satiety)
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Miguel, N; Journal of Neurochemistry 1996, V67(5), P1982
(2) Novo Nordisk AS; WO 9731943 A1 1997 HCAPLUS
(3) Turton, M; Nature 1996, V379, P69 HCAPLUS

L58 ANSWER 14 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:163616 HCAPLUS
DN 128:244341
ED Entered STN: 19 Mar 1998
TI Preparation of lipophilic human **glucagon**-like peptide-1 derivatives with protracted action profiles
IN Knudsen, Liselotte Bjerre; Sorensen, Per Olaf; Nielsen, Per Franklin
PA Novo Nordisk A/S, Den.; Knudsen, Liselotte Bjerre; Sorensen, Per Olaf; Nielsen, Per Franklin
SO PCT Int. Appl., 76 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07K014-605
ICS A61K038-26
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): **1**
FAN.CNT 12

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9808871	A1	19980305	WO 1997-DK340	19970822 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9738478	A1	19980319	AU 1997-38478	19970822 <--

PI AU 732957 B2 20010503
EP 944648 A1 19990929 EP 1997-935509 19970822 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO
CN 1232470 A 19991020 CN 1997-198413 19970822 <--
BR 9711437 A 20000118 BR 1997-11437 19970822 <--
JP 2000500505 T2 20000118 JP 1998-511183 19970822 <--
JP 3149958 B2 20010326
JP 2001011095 A2 20010116 JP 2000-152778 19970822 <--
RU 2214419 C2 20031020 RU 1999-106518 19970822 <--
ZA 9707791 A 19980302 ZA 1997-7791 19970829 <--
ZA 9707828 A 19980302 ZA 1997-7828 19970901 <--
NO 9900950 A 19990428 NO 1999-950 19990226 <--
US 6268343 B1 20010731 US 1999-258750 19990226 <--
KR 2000035964 A 20000626 KR 1999-701750 19990302 <--
US 2001011071 A1 20010802 US 1999-398111 19990916 <--
US 6458924 B2 20021001
US 2002025933 A1 20020228 US 2001-908534 20010718 <--
US 2003199672 A1 20031023 US 2002-285079 20020819 <--
PRAI DK 1996-931 A 19960830 <--
DK 1996-1259 A 19961108 <--
DK 1996-1470 A 19961220 <--
US 1997-35904P P 19970124 <--
US 1997-35905P P 19970124 <--
US 1997-36255P P 19970124 <--
US 1997-36226P P 19970125 <--
JP 1998-511183 A3 19970822 <--
WO 1997-DK340 W 19970822 <--
US 1997-918810 B2 19970826 <--
US 1997-922200 B2 19970902 <--
DK 1998-263 A 19980227 <--
DK 1998-264 A 19980227 <--
DK 1998-268 A 19980227 <--
DK 1998-271 A 19980227 <--
DK 1998-272 A 19980227 <--
DK 1998-274 A 19980227 <--
US 1998-38432 B2 19980311 <--
EP 1998-610006 A 19980313 <--
US 1998-78422P P 19980318 <--
DK 1998-507 A 19980408 <--
DK 1998-508 A 19980408 <--
DK 1998-509 A 19980408 <--
US 1998-82478P P 19980421 <--
US 1998-82479P P 19980421 <--
US 1998-82480P P 19980421 <--
US 1998-84357P P 19980421 <--
US 1998-82802P P 19980423 <--
US 1998-85789P P 19980518 <--
US 1999-258187 B1 19990225
US 1999-258750 A2 19990226
US 1999-265141 A2 19990308
US 1999-398111 A1 19990916

AB Lipophilic human **glucagon**-like peptide-1 (GLP-1) derivs. and analogs thereof having a lipophilic substituent have interesting pharmacol. properties, in particular they have a more protracted profile of action than GLP-1(7-37). Thus, coupling of GLP-1(7-37)-OH with Me(CH2)12CO-Glu(OSu)-OCMe3 (Su = succinimidyl) (preparation given), followed by deesterification with CF3CO2H and chromatog. purification gave 8% bis-adduct Lys[Me(CH2)12CO-γ-Glu]26,34-GLP-1(7-37)-OH (NNC 90-1167). Several prepared lipophilic GLP-1 analogs were tested for protracted plasma concentration in pigs and were found to be much more persistent than GLP-1(7-37). In addition, the time of peak plasma concentration was found to vary within wide limits

depending on the particular lipophilic GLP-1 derivative selected. The efficacy of several prepared derivs. was tested by stimulation of cAMP in a cell line expressing cloned human GLP-1 receptor.

ST lipophilic **glucagon** like peptide prepn antidiabetic; antiobesity agent lipophilic **glucagon** like peptide

IT Carboxylic acids, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(dicarboxylic, long-chain, **glucagon**-like peptide conjugates; preparation of lipophilic human **glucagon**-like peptide-1 derivs. with protracted action profiles)

IT Fatty acids, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**glucagon**-like peptide conjugates; preparation of lipophilic human **glucagon**-like peptide-1 derivs. with protracted action profiles)

IT Antidiabetic agents
Antiobesity agents
(preparation of lipophilic human **glucagon**-like peptide-1 derivs. with protracted action profiles)

IT **106612-94-6**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); **THU (Therapeutic use)**; BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(preparation of lipophilic human **glucagon**-like peptide-1 derivs. with protracted action profiles)

IT **87805-34-3DP, Glucagon**-like peptide I (human), lipophilic derivs. **89750-14-1DP, Glucagon**-related peptide I, lipophilic derivs. 99658-04-5DP, lipophilic derivs. **104364-62-7DP, Glucagon**-related peptide I (guinea pig clone gpGCG-2), lipophilic derivs. **106612-94-6DP, Glucagon**-like peptide I(7-37) (human), lipophilic derivs. 107444-51-9DP, lipophilic derivs. 121181-17-7DP, **Glucagon**-related peptide 1 (Octodon degus), lipophilic derivs. 123475-27-4DP, lipophilic derivs. **123475-28-5DP**, lipophilic derivs. 123512-62-9DP, lipophilic derivs. **157569-66-9DP**, lipophilic derivs. **157629-57-7DP**, lipophilic derivs. **204521-54-0P** **204521-55-1P** 204521-56-2P **204521-57-3P** **204521-58-4P** 204521-59-5P **204521-68-6DP**, lipophilic derivs. **204521-69-7DP**, lipophilic derivs. **204521-70-0DP**, lipophilic derivs. **204521-72-2DP**, lipophilic derivs. **204521-81-3DP**, lipophilic derivs. **204521-82-4DP**, lipophilic derivs. **204521-83-5DP**, lipophilic derivs. **204521-84-6DP**, lipophilic derivs. **204521-85-7DP**, lipophilic derivs. **204521-86-8DP**, lipophilic derivs. **204521-87-9DP**, lipophilic derivs. **204521-88-0DP**, lipophilic derivs. **204521-89-1DP**, lipophilic derivs. **204521-90-4DP**, lipophilic derivs. **204521-91-5DP**, lipophilic derivs. **204521-92-6DP**, lipophilic derivs. **204655-84-5DP**, lipophilic derivs. **204655-85-6DP**, lipophilic derivs. **204655-86-7DP**, lipophilic derivs. **204655-87-8P** **204655-88-9P** **204655-89-0DP**, lipophilic derivs. **204655-90-3DP**, lipophilic derivs. **204655-91-4DP**, lipophilic derivs. **204655-92-5DP**, lipophilic derivs. **204655-93-6DP**, lipophilic derivs. **204655-94-7P** **204655-96-9P** 204655-97-0P **204655-98-1P** **204655-99-2P** **204656-00-8P** **204656-01-9P** 204656-02-0P **204656-03-1DP**, lipophilic derivs. **204656-04-2DP**, lipophilic derivs. **204656-05-3DP**, lipophilic derivs. **204656-06-4DP**, lipophilic derivs.

204656-07-5DP, lipophilic derivs. 204656-08-6P
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204656-66-6DP, lipophilic derivs. 204656-67-7DP,
lipophilic derivs. 204656-68-8DP, lipophilic derivs.
204656-69-9DP, lipophilic derivs. 204656-70-2DP,
lipophilic derivs. 204656-71-3DP, lipophilic derivs.
204656-72-4DP, lipophilic derivs. 204656-73-5DP,
lipophilic derivs. 204656-74-6DP, lipophilic derivs.
204656-75-7DP, lipophilic derivs. 204656-76-8DP,
lipophilic derivs. 204656-77-9DP, lipophilic derivs.
204656-78-0DP, lipophilic derivs. 204656-79-1DP,
lipophilic derivs. 204656-80-4DP, lipophilic derivs.
204656-81-5DP, lipophilic derivs. 204656-82-6DP,
lipophilic derivs. 204656-83-7DP, lipophilic derivs.
204656-84-8DP, lipophilic derivs. 204656-85-9DP,
lipophilic derivs. 204656-86-0DP, lipophilic derivs.
204656-87-1DP, lipophilic derivs. 204656-88-2DP,
lipophilic derivs. 204656-89-3DP, lipophilic derivs.
204656-90-6DP, lipophilic derivs. 204656-91-7DP,
lipophilic derivs. 204656-92-8DP, lipophilic derivs.
204656-93-9DP, lipophilic derivs. 204656-94-0DP,
lipophilic derivs. 204656-95-1DP, lipophilic derivs.
204656-96-2DP, lipophilic derivs. 204656-97-3DP,
lipophilic derivs. 204996-97-4P, NNC 901167
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of lipophilic human **glucagon**-like peptide-1 derivs. with protracted action profiles)

IT 434-13-9, Lithocholic acid 14464-31-4 14464-32-5 45120-30-7,
L-Glutamic acid α-tert-butyl ester 69888-86-4 128746-57-6
146004-82-2 146004-83-3 146004-84-4 146004-85-5 204521-68-6
204521-69-7 204521-70-0 204521-71-1 204521-72-2 204521-73-3
204521-75-5 204655-83-4 204655-95-8
RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of lipophilic human **glucagon**-like peptide-1 derivs. with protracted action profiles)
IT 104211-94-1P 204521-61-9P 204521-63-1P 204521-65-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of lipophilic human **glucagon**-like peptide-1 derivs. with protracted action profiles)
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Buckley, D; WO 9111457 A1 1991 HCAPLUS
(2) Chen, V; US 5512549 A 1996 HCAPLUS
(3) London Health Association; WO 9531214 A1 1995 HCAPLUS

L58 ANSWER 15 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:41714 HCAPLUS
DN 128:111161
ED Entered STN: 24 Jan 1998
TI **Glucagon**-like insulinotropic peptides, compositions and methods
IN Galloway, John A.; Hoffmann, James A.
PA Eli Lilly and Company, USA
SO U.S., 8 pp., Cont.-in-part of U.S. Ser. No. 164,277, abandoned.
CODEN: USXXAM
DT Patent
LA English
IC ICM A61K038-26
ICS C07K014-605
NCL 514012000
CC 2-6 (Mammalian Hormones)
Section cross-reference(s): **63**
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5705483	A	19980106	US 1995-407831	19950321 <--
	CA 2137206	AA	19950610	CA 1994-2137206	19941202 <--
	JP 07196695	A2	19950801	JP 1994-303404	19941207 <--
	IN 178440	A	19970426	IN 1995-CA495	19950502 <--
	ZA 9504141	A	19961122	ZA 1995-4141	19950522 <--
	TW 389769	B	20000511	TW 1995-84105110	19950522 <--
	IL 113809	A1	20000726	IL 1995-113809	19950522 <--
	NO 9502034	A	19960923	NO 1995-2034	19950523 <--
	EP 733644	A1	19960925	EP 1995-303423	19950523 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	HU 74729	A2	19970228	HU 1995-1508	19950523 <--
	EP 1364967	A2	20031126	EP 2003-13464	19950523 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV				
	CA 2150080	AA	19960922	CA 1995-2150080	19950524 <--
	FI 9502536	A	19960922	FI 1995-2536	19950524 <--
	AU 9520268	A1	19961003	AU 1995-20268	19950524 <--
	AU 708159	B2	19990729		
	RU 2147588	C1	20000420	RU 1995-108231	19950525 <--
	PL 182113	B1	20011130	PL 1995-308783	19950525 <--
	CN 1131674	A	19960925	CN 1995-105569	19950526 <--
	JP 08269097	A2	19961015	JP 1995-127910	19950526 <--
	JP 2003048899	A2	20030221	JP 2002-204749	19950526 <--
	BR 9503036	A	19970923	BR 1995-3036	19950630 <--
	US 5977071	A	19991102	US 1997-927227	19970910 <--
	US 6133235	A	20001017	US 1999-348136	19990706 <--
	US 6410513	B1	20020625	US 2000-573809	20000518 <--
	US 6388053	B1	20020514	US 2001-975905	20011012 <--
	US 2002165342	A1	20021107	US 2002-125255	20020417 <--
	JP 2004002480	A2	20040108	JP 2003-312979	20030904 <--
PRAI	US 1993-164277	B2	19931209 <--		

US 1995-407831	A	19950321	<--
EP 1995-303423	A3	19950523	<--
JP 1995-127910	A3	19950526	<--
US 1997-927227	A3	19970910	<--
US 1999-348136	A1	19990706	
US 2000-573809	A1	20000518	
US 2001-975905	A1	20011012	

OS MARPAT 128:111161

AB The present invention provides novel complexes consisting of certain GLP-1 mols. associated with a divalent metal cation that is capable of co-precipitating with a GLP-1 mol. Pharmaceutical compns. and methods of using such complexes for enhancing the expression of insulin in B-type islet cells is claimed, as is a method for treating maturity onset diabetes mellitus in mammals, particularly humans.

ST GLP1 metal complex prepn insulinotropic

IT Cations
(divalent, complexes, with GLP-1 analogs; preparation and formulation of **glucagon**-like insulinotropic peptides)

IT Diabetes mellitus
(non-insulin-dependent; preparation and formulation of **glucagon**-like insulinotropic peptides)

IT Antidiabetic agents
Drug delivery systems
(preparation and formulation of **glucagon**-like insulinotropic peptides)

IT Coordination compounds
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(with GLP-1 analogs; preparation and formulation of **glucagon**-like insulinotropic peptides)

IT 7440-66-6DP, Zinc, complexes with GLP-1 analogs, biological studies
7646-85-7DP, Zinc chloride, complexes with GLP-1 analogs
89750-14-1DP, **Glucagon**-related peptide I, analogs, divalent metal complexes 107444-51-9DP, Human **glucagon** like peptide-1 (7-36) amide, complexes with divalent cations
194551-05-8DP, complexes with divalent metal cations
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and formulation of **glucagon**-like insulinotropic peptides)

IT 9004-10-8, Insulin, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(preparation and formulation of **glucagon**-like insulinotropic peptides)

RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Altman, J; Synthetic Commun 1989, V19(11 & 12), P2069
(2) Ananthanancayanan, V; Mol Biol Cell (Supp) 1992, V3, P250A
(3) Anon; WO 9111457 1991 HCAPLUS
(4) Anon; WO 9218531 1992 HCAPLUS
(5) Anon; WO 9318786 1993 HCAPLUS
(6) Anon; WO 9325579 1993 HCAPLUS
(7) Anon; WO 9505848 1994
(8) Anon; WO 9505848 1995
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(16) Hasselblatt; Handbook of Experimental Pharmacology 1975, V32(2), P729
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(23) Nauck, M; Diabetologia 1993, V36, P741 MEDLINE
(24) Nauck, M; J Clin Invest 1993, V91, P301 MEDLINE
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(26) Orskov, C; J Biol Chem 1989, V264(22), P12826 MEDLINE
(27) Owa, T; Chem Letters 1988, P873
(28) O'Donnell, M; Synthetic Commun 1989, V19(7 & 8), P1157
(29) Pridal, L; International Journal of Pharmaceutics 1996, V136, P53 HCAPLUS
(30) Suzuki, S; Endocrinology 1990, V125, P3109
(31) Thorens, B; Diabetes 1993, V42, P1219 HCAPLUS

L58 ANSWER 16 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:542509 HCAPLUS
DN 127:201022
ED Entered STN: 25 Aug 1997
TI **Glucagon**-like peptide 1-based protein heterologous expression in transformed mammal cell line, gene therapy of diabetes, and transformed cell line implants
IN Borts, Tracy L.; Broderick, Carol L.; Dimarchi, Richard D.; Grinnell, Brian W.; Miller, Anne R.
PA Eli Lilly and Co., USA; Borts, Tracy L.; Broderick, Carol L.; Dimarchi, Richard D.; Grinnell, Brian W.; Miller, Anne R.
SO PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12N005-00
ICS C12N015-00; C12N015-16; C12N015-09; A61K048-00
CC 3-2 (Biochemical Genetics)
Section cross-reference(s): 1, 2, 14
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9729180	A1	19970814	WO 1997-US1978	19970206	<--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
	CA 2243718	AA	19970814	CA 1997-2243718	19970206	<--
	AU 9722631	A1	19970828	AU 1997-22631	19970206	<--
	EP 879279	A1	19981125	EP 1997-905834	19970206	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI, RO					
	JP 2001503963	T2	20010327	JP 1997-528685	19970206	<--
PRAI	US 1996-12111P	P	19960206	<--		
	GB 1996-3847	A	19960223	<--		
	WO 1997-US1978	W	19970206	<--		

OS MARPAT 127:201022
AB The invention provides a gene therapy method for delivering safe and effective, long-term amts. of **glucagon**-like peptide 1 GLP-1(7-37)-based proteins useful for treating Type I and Type II

diabetes. The invention eliminates the need for s.c. injections and is able to provide tight glucose control. Plasmid vectors containing GLP-1 were constructed and pGT-h+tLB+GLP-1, pGT-h+tLB+Val8GLP-1, or pMT-h+tLB+Val8GLP-1 was transfected into human embryonic kidney cells. Monoclonal cell lines were screened for the ability to secrete GLP-1(7-37)-based protein into the culture medium. Transformed 293 cells were cultured then surgically transplanted under the kidney capsule of 8 wk old Zucker Diabetic Fatty male rats.

ST **glucagon** like peptide 1 diabetes therapy; gene therapy GLP 1 peptide recombinant; implant recombinant cell GLP 1 diabetes

IT Animal cell line
(293; **glucagon**-like peptide 1-based protein heterologous expression in transformed mammal cell line, gene therapy of diabetes, and transformed cell line implants)

IT Metallothioneins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(gene promoter, in vector; **glucagon**-like peptide 1-based protein heterologous expression in transformed mammal cell line, gene therapy of diabetes, and transformed cell line implants)

IT Animal cell line
DNA sequences
Genetic vectors
Immunosuppressants
Immunotherapy
Mammal (Mammalia)
Plasmid vectors
Protein sequences
Transformation, genetic
Transplant and Transplantation
(**glucagon**-like peptide 1-based protein heterologous expression in transformed mammal cell line, gene therapy of diabetes, and transformed cell line implants)

IT Promoter (genetic element)
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in vector; **glucagon**-like peptide 1-based protein heterologous expression in transformed mammal cell line, gene therapy of diabetes, and transformed cell line implants)

IT Diabetes mellitus
(insulin-dependent; **glucagon**-like peptide 1-based protein heterologous expression in transformed mammal cell line, gene therapy of diabetes, and transformed cell line implants)

IT Diabetes mellitus
(non-insulin-dependent; **glucagon**-like peptide 1-based protein heterologous expression in transformed mammal cell line, gene therapy of diabetes, and transformed cell line implants)

IT Plasmid vectors
(pGT-h+tLB+GLP-1; **glucagon**-like peptide 1-based protein heterologous expression in transformed mammal cell line, gene therapy of diabetes, and transformed cell line implants)

IT Plasmid vectors
(pGT-h+tLB+Val8GLP-1; **glucagon**-like peptide 1-based protein heterologous expression in transformed mammal cell line, gene therapy of diabetes, and transformed cell line implants)

IT Plasmid vectors
(pMT-h+tLB+Val8GLP-1; **glucagon**-like peptide 1-based protein heterologous expression in transformed mammal cell line, gene therapy of diabetes, and transformed cell line implants)

IT Virus
(promoter, in vector; **glucagon**-like peptide 1-based protein heterologous expression in transformed mammal cell line, gene therapy of diabetes, and transformed cell line implants)

IT Secretion (process)
(protein; **glucagon**-like peptide 1-based protein heterologous expression in transformed mammal cell line, gene therapy of diabetes, and transformed cell line implants)
IT **194551-05-8P**
RL: BPN (Biosynthetic preparation); PRP (Properties); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; **glucagon**-like peptide 1-based protein heterologous expression in transformed mammal cell line, gene therapy of diabetes, and transformed cell line implants)
IT **106612-94-6P**, Rat GLP-I(7-37)
RL: BPN (Biosynthetic preparation); PRP (Properties); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(**glucagon**-like peptide 1-based protein heterologous expression in transformed mammal cell line, gene therapy of diabetes, and transformed cell line implants)
IT 194616-47-2 194616-48-3
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(nucleotide sequence; **glucagon**-like peptide 1-based protein heterologous expression in transformed mammal cell line, gene therapy of diabetes, and transformed cell line implants)

L58 ANSWER 17 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:485850 HCAPLUS
DN 125:134810
ED Entered STN: 16 Aug 1996
TI Production of peptides using recombinant carbonic anhydrase fusion protein constructs
IN Partridge, Bruce E.; Stout, Jay S.; Henriksen, Dennis B.; Manning, Shane D.; De La Motte, Rebecca S.; Holmquist, Barton; Wagner, Fred W.
PA Bionebraska, Inc., USA
SO PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12N015-62
ICS C12N009-88; C07K014-60; C07K014-605; C07K014-635; C07K001-30; C07K001-113
CC 3-2 (Biochemical Genetics)
Section cross-reference(s): **1**, 34
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9617942	A1	19960613	WO 1995-US15800	19951207 <--
	W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2206848	AA	19960613	CA 1995-2206848	19951207 <--
	AU 9644158	A1	19960626	AU 1996-44158	19951207 <--
	AU 700605	B2	19990107		
	EP 796335	A1	19970924	EP 1995-942995	19951207 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 10510155	T2	19981006	JP 1996-517724	19951207 <--
PRAI	US 1994-350530	A	19941207 <--		
	WO 1995-US15800	W	19951207 <--		

AB A method for the isolation and/or purification of a recombinant peptide by employing a fusion protein construct which includes a carbonic anhydrase and a variable fused polypeptide is provided. The method includes precipitating either the fusion protein construct or a fragment of the fusion protein construct including the carbonic anhydrase. Inclusion bodies which includes the fusion protein construct and a method of producing a peptide which includes expressing the fusion protein construct as a part of an inclusion body are also provided. Fusion protein constructs which include a carbonic anhydrase and certain target peptides are also provided.

ST carbonic anhydrase fusion recombinant peptide prodn

IT Staphylococcus aureus
(V8, cleaving agent; production of peptides using recombinant carbonic anhydrase fusion protein constructs)

IT Escherichia coli
(host cell; production of peptides using recombinant carbonic anhydrase fusion protein constructs)

IT Surfactants
(precipitant; production of peptides using recombinant carbonic anhydrase fusion protein constructs)

IT Inclusion bodies
(production of peptides using recombinant carbonic anhydrase fusion protein constructs)

IT Peptides, biological studies
RL: BPN (Biosynthetic preparation); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(production of peptides using recombinant carbonic anhydrase fusion protein constructs)

IT Enzymes
RL: CAT (Catalyst use); USES (Uses)
(ubiquitin-cleaving; production of peptides using recombinant carbonic anhydrase fusion protein constructs)

IT Chromatography, column and liquid
(affinity, production of peptides using recombinant carbonic anhydrase fusion protein constructs)

IT Precipitation
(agents, production of peptides using recombinant carbonic anhydrase fusion protein constructs)

IT Denaturants
(chaotropic, precipitant; production of peptides using recombinant carbonic anhydrase fusion protein constructs)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(fusion products, with carbonic anhydrase; production of peptides using recombinant carbonic anhydrase fusion protein constructs)

IT Substitution reaction
(thiocyanation, production of peptides using recombinant carbonic anhydrase fusion protein constructs)

IT 163912-67-2P
RL: BPN (Biosynthetic preparation); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(GLP1 (1-34); production of peptides using recombinant carbonic anhydrase fusion protein constructs)

IT **127650-06-0P**
RL: BPN (Biosynthetic preparation); PUR (Purification or recovery); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(GLP1 (7-34); production of peptides using recombinant carbonic anhydrase

fusion protein constructs)
IT 123475-27-4P
RL: BPN (Biosynthetic preparation); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(GLP1 (7-36); production of peptides using recombinant carbonic anhydrase fusion protein constructs)
IT 179765-26-5P
RL: BPN (Biosynthetic preparation); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(GLP1 (7-37); production of peptides using recombinant carbonic anhydrase fusion protein constructs)
IT 163912-74-1P, 1-41-Somatoliberin (human pancreatic islet)
RL: BPN (Biosynthetic preparation); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(GRF (1-41); production of peptides using recombinant carbonic anhydrase fusion protein constructs)
IT 90599-39-6P
RL: BPN (Biosynthetic preparation); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(GRF (1-44); production of peptides using recombinant carbonic anhydrase fusion protein constructs)
IT 52232-67-4P
RL: BPN (Biosynthetic preparation); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(PTH (1-34); production of peptides using recombinant carbonic anhydrase fusion protein constructs)
IT 179800-18-1P
RL: BPN (Biosynthetic preparation); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(PTH (1-38); production of peptides using recombinant carbonic anhydrase fusion protein constructs)
IT 75-05-8, Acetonitrile, uses 77-92-9, uses 25322-68-3 62309-51-7, Propanol
RL: NUU (Other use, unclassified); USES (Uses)
(organic solvent; production of peptides using recombinant carbonic anhydrase
fusion protein constructs)
IT 50-01-1, Guanidine hydrochloride 57-13-6, Urea, uses 7757-82-6, Sodium sulfate, uses 7783-20-2, Ammonium sulfate, uses
RL: NUU (Other use, unclassified); USES (Uses)
(precipitant; production of peptides using recombinant carbonic anhydrase fusion protein constructs)
IT 9001-03-0DP, Carbonic anhydrase, fusion products with protein
RL: BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(production of peptides using recombinant carbonic anhydrase fusion protein constructs)
IT 9002-64-6P, Parathormone 9034-39-3P, Growth hormone releasing factor 86546-19-2P **89750-14-1P**, **Glucagon**-related peptide I
RL: BPN (Biosynthetic preparation); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(production of peptides using recombinant carbonic anhydrase fusion protein constructs)
IT 506-68-3, Cyanogen bromide 7803-49-8, Hydroxylamine, uses 9001-92-7,

Endopeptidase 9002-04-4, Thrombin 9002-05-5, Blood coagulation factor Xa 9002-07-7, Trypsin 9004-07-3, Chymotrypsin 9014-01-1, Subtilisin 9014-74-8, Enterokinase 9015-94-5, Renin, uses 9028-00-6, Clostripain 9046-67-7, Carboxypeptidase y 27933-36-4, BNPS-skatole
RL: CAT (Catalyst use); USES (Uses)
(production of peptides using recombinant carbonic anhydrase fusion protein constructs)

IT 59-66-5D, Acetazolamide, compds. 98-10-2D, Benzenesulfonamide, compds.
RL: NUU (Other use, unclassified); USES (Uses)
(support; production of peptides using recombinant carbonic anhydrase fusion protein constructs)

L58 ANSWER 18 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:483657 HCAPLUS
DN 125:134811
ED Entered STN: 15 Aug 1996
TI Production of C-terminal amidated peptides from recombinant protein constructs and therapeutic applications
IN Stout, Jay S.; Patridge, Bruce E.; Heriksen, Dennis B.; Holmquist, Barton; Wagner, Fred W.
PA Bionebraska, Inc., USA
SO PCT Int. Appl., 91 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12N015-62
ICS C12N015-16; C12N015-60; C07K001-113; C12P021-06; C07K014-635; C07K014-60; C07K014-605; C07K007-22; C12N001-21
CC 3-2 (Biochemical Genetics)
Section cross-reference(s): 1, 10, 16, 34
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9617941	A2	19960613	WO 1995-US15799	19951207 <--
	WO 9617941	A3	19960822		
	W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9644157	A1	19960626	AU 1996-44157	19951207 <--
	US 6051399	A	20000418	US 1997-934171	19970919 <--
PRAI	US 1994-350528		19941207 <--		
	WO 1995-US15799		19951207 <--		

AB A method for the production of C-terminal amidated recombinant peptides is provided. The method employs a recombinant protein construct having multiple copies of a target peptide linked by intraconnecting peptides. The intraconnecting peptides permit the multicopy construct to be selectively reacted to produce product peptides having a C-terminal α-carboxamide. A recombinant gene containing a DNA sequence coding for the recombinant protein construct and an expression cassette, an expression vector and a transformed cell including the recombinant gene are also provided.
ST amidated peptide prodn recombinant construct therapeutic
IT Staphylococcus aureus
(V8; production of C-terminal amidated peptides from recombinant protein constructs and therapeutic applications)
IT Proteins, biological studies
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(glycine-containing, peptide multicopy construct; production of C-terminal amidated peptides from recombinant protein constructs and therapeutic applications)

IT Proteins, biological studies
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(homoserine-containing, peptide multicopy construct; production of C-terminal amidated peptides from recombinant protein constructs and therapeutic applications)

IT Escherichia coli
(host cell; production of C-terminal amidated peptides from recombinant protein constructs and therapeutic applications)

IT Inclusion bodies
(isolation of recombinant protein construct-containing inclusion body; production of C-terminal amidated peptides from recombinant protein constructs and therapeutic applications)

IT Antigens
Proteins, biological studies
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(peptide multicopy construct; production of C-terminal amidated peptides from recombinant protein constructs and therapeutic applications)

IT Gene
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(peptide multicopy construct; production of C-terminal amidated peptides from recombinant protein constructs and therapeutic applications)

IT Fermentation
Genetic vectors
Molecular cloning
(production of C-terminal amidated peptides from recombinant protein constructs and therapeutic applications)

IT Aromatic compounds
RL: CAT (Catalyst use); USES (Uses)
(thiocyanato-, S-cyanylating agent; production of C-terminal amidated peptides from recombinant protein constructs and therapeutic applications)

IT Enzymes
RL: CAT (Catalyst use); USES (Uses)
(ubiquitin-cleaving, cleavage reagent; production of C-terminal amidated peptides from recombinant protein constructs and therapeutic applications)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(DNA-binding, peptide multicopy construct; production of C-terminal amidated peptides from recombinant protein constructs and therapeutic applications)

IT Peptides, biological studies
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amides, production of C-terminal amidated peptides from recombinant protein constructs and therapeutic applications)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(arginine-containing, peptide multicopy construct; production of C-terminal amidated peptides from recombinant protein constructs and therapeutic applications)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cysteine-containing, peptide multicopy construct; production of C-terminal amidated peptides from recombinant protein constructs and therapeutic applications)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(histidine-rich, peptide multicopy construct; production of C-terminal amidated peptides from recombinant protein constructs and therapeutic applications)

IT Proteins, specific or class, biological studies
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(ligand-binding, peptide multicopy construct; production of C-terminal amidated peptides from recombinant protein constructs and therapeutic applications)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(methionine-containing, peptide multicopy construct; production of C-terminal amidated peptides from recombinant protein constructs and therapeutic applications)

IT Genetic element
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(promoter, production of C-terminal amidated peptides from recombinant protein constructs and therapeutic applications)

IT Substitution reaction
(thiocyanation, production of C-terminal amidated peptides from recombinant protein constructs and therapeutic applications)

IT Amidation
(trans-, precursor peptide transamidation in exopeptidase presence; production of C-terminal amidated peptides from recombinant protein constructs and therapeutic applications)

IT 90597-47-0, PeptidylGlycine monooxygenase
RL: CAT (Catalyst use); USES (Uses)
(C-terminal glycine decomposition to form amidated peptide; production of C-terminal amidated peptides from recombinant protein constructs and therapeutic applications)

IT **123475-28-5P**
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); PRP (Properties); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(GLP1 (7-35), target peptide; production of C-terminal amidated peptides from recombinant protein constructs and therapeutic applications)

IT 90599-39-6P
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(GRF (1-44), target peptide; production of C-terminal amidated peptides from recombinant protein constructs and therapeutic applications)

IT 52232-67-4P
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified);

PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(PTH (1-34) target peptide; production of C-terminal amidated peptides from recombinant protein constructs and therapeutic applications)

IT 30211-77-9, 2-Nitro-5-thiocyanatobenzoic acid 59016-56-7, 1-Cyano-4-(dimethylamino)pyridinium tetrafluoroborate 179695-01-3 179695-03-5
RL: CAT (Catalyst use); USES (Uses)
(S-cyanylating agent; production of C-terminal amidated peptides from recombinant protein constructs and therapeutic applications)

IT 506-68-3, Cyanogen bromide 9001-33-6, Ficin 9001-73-4, Papain 9001-92-7, Endopeptidase 9002-04-4, Thrombin 9002-05-5, Blood coagulation factor Xa 9002-07-7, Trypsin 9004-07-3, Chymotrypsin 9014-01-1, Subtilisin 9014-74-8, Enterokinase 9015-94-5, Renin, uses 9028-00-6, Clostripain
RL: CAT (Catalyst use); USES (Uses)
(cleavage reagent; production of C-terminal amidated peptides from recombinant protein constructs and therapeutic applications)

IT 9001-03-0P, Carbonic anhydrase
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(peptide multicopy construct; production of C-terminal amidated peptides from recombinant protein constructs and therapeutic applications)

IT 9031-96-3, Exopeptidase
RL: CAT (Catalyst use); USES (Uses)
(precursor peptide transamidation in exopeptidase presence; production of C-terminal amidated peptides from recombinant protein constructs and therapeutic applications)

IT 1904-78-5, 2-Nitrobenzylamine 9031-98-5, Carboxypeptidase 9046-67-7, Carboxypeptidase Y
RL: CAT (Catalyst use); USES (Uses)
(precursor peptide transamidation; production of C-terminal amidated peptides from recombinant protein constructs and therapeutic applications)

IT 14280-30-9, Hydroxide, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction with S-cyanylated peptide to produce precursor peptide; production of C-terminal amidated peptides from recombinant protein constructs and therapeutic applications)

IT 33507-63-0P, Substance P
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target peptide; production of C-terminal amidated peptides from recombinant protein constructs and therapeutic applications)

L58 ANSWER 19 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:621604 HCAPLUS
DN 123:28218
ED Entered STN: 20 Jun 1995
TI Enzymatic method for modification of recombinant polypeptides
IN Wagner, Fred W.; Stout, Jay; Henriksen, Dennis; Partridge, Bruce; Manning, Shane
PA Bionebraska, Inc., USA
SO PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12N015-11
ICS C12P021-06; C07K014-605; C07K014-60; C12N001-21; A61K038-20; A61K038-22
CC 6-3 (General Biochemistry)

Section cross-reference(s): 1, 9

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9503405	A2	19950202	WO 1994-US8125	19940719	<--
	WO 9503405	A3	19950316			
	W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UZ, VN					
	RW: KE, MW, SD, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
	US 5512459	A	19960430	US 1993-95162	19930720	<--
	CA 2166870	AA	19950202	CA 1994-2166870	19940719	<--
	AU 9480094	A1	19950220	AU 1994-80094	19940719	<--
	AU 693815	B2	19980709			
	JP 09500279	T2	19970114	JP 1994-505268	19940719	<--
	EP 789760	A2	19970820	EP 1994-931264	19940719	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE					
	US 5707826	A	19980113	US 1995-470220	19950606	<--
	US 6037143	A	20000314	US 1997-967374	19971107	<--
	US 6403361	B1	20020611	US 2000-505991	20000217	<--

PRAI	US 1993-95162	A	19930720	<--
	WO 1994-US8125	W	19940719	<--
	US 1995-470220	A3	19950606	<--
	US 1995-520485	B1	19950829	<--
	US 1997-967374	A1	19971107	<--

AB An enzymic method is provided for the formation of a recombinant polypeptide which has been modified at the C-terminal end through the use of a transpeptidation process. The method is suitable for modifying recombinant polypeptides of any source including those which may be com. available, those derived from recombinant single copy or multi-copy polypeptide constructs, or those derived from single or multi-copy recombinant fusion proteins constructs. The transpeptidation reaction involves contacting an endopeptidase enzyme with a recombinant polypeptide to substitute and addition unit, of one or more acids, for leaving unit, linked to a core polypeptide through a cleavage site recognized by the endopeptidase enzyme. Recombinant polypeptides derived from multi-copy polypeptide constructs may be cleaved from the multi-copy polypeptide at the N-terminal and C-terminal ends and simultaneously undergo substitution of the leaving unit by the desired addition unit. The invention utilizes known and newly discovered cleavage recognition sites of effectuate the desired modification products. Preparation of C-terminally amidated **glucagon** like peptide 1 and growth hormone releasing factor using trypsin and thrombin, resp., as an endopeptidase was demonstrated.

ST recombinant peptide carboxy terminus amidation

IT Antidiabetics and Hypoglycemics
(C-terminally amidated **glucagon** like peptide 1 for)

IT Osteoporosis
(C-terminally amidated growth hormone releasing factor for treatment of)

IT Escherichia coli
(fusion protein prepared in transgenic Escherichia coli for modification via transpeptidation)

IT Eukaryote
(fusion protein prepared in transgenic eukaryotes for modification via transpeptidation)

IT Prokaryote
(fusion protein prepared in transgenic prokaryotes for modification via transpeptidation)

IT Animal growth
(disorder, short-stature, C-terminally amidated growth hormone releasing factor for treatment of)

IT Uterus, disease

(endometriosis, C-terminally amidated growth hormone releasing factor for treatment of)

IT Amidation
(trans-, enzymic method for modification of recombinant polypeptides by transpeptidation)

IT 163912-67-2P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation)
(1-34-**Glucagon** like peptide 1; enzymic method for C-terminally amidation of)

IT 163912-74-1P, 1-41-Somatoliberin (human pancreatic islet)
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation)
(1-41-growth hormone releasing factor; enzymic method for C-terminally amidation of)

IT 83930-13-6P, Somatoliberin (human pancreatic islet)
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation)
(1-44-growth hormone releasing factor derivative; enzymic method for C-terminally amidation of)

IT **127650-06-0P**
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation)
(7-34-**Glucagon** like peptide 1; enzymic method for C-terminally amidation of)

IT **89750-14-1P**, **Glucagon**-related peptide I
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation)
(enzymic method for amidation of C-terminus of **glucagon** like peptide 1)

IT 9034-39-3P, Growth hormone releasing factor
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation)
(enzymic method for amidation of C-terminus of growth hormone releasing factor)

IT 106612-94-6P 107444-51-9P 119637-73-9P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation)
(**glucagon** like peptide 1 derivative; enzymic method for C-terminally amidation of)

IT 9001-03-0D, Carbonic anhydrase, fusion products with **glucagon** like peptide 1
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(in enzymic amidation of C-terminus of **glucagon** like peptide 1)

IT 9001-33-6, Ficin 9001-73-4, Papain 9001-92-7, Endopeptidase 9002-04-4, Thrombin 9002-07-7, Trypsin 9004-07-3, Chymotrypsin 9013-55-2, Blood-coagulation factor XI 9014-01-1, Subtilisin 9014-74-8, Enterokinase 37259-58-8, Serine endopeptidase 37353-41-6, Cysteine endopeptidase
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(in enzymic method for modification of recombinant polypeptides by transpeptidation)

IT 163918-02-3 163918-03-4
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(in modification of recombinant polypeptides by transpeptidation using thrombin)

IT 24326-03-2 55033-47-1
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(in modification of recombinant polypeptides by transpeptidation using trypsin)

L58 ANSWER 20 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:257836 HCAPLUS
DN 122:38834
ED Entered STN: 22 Dec 1994
TI Prolonged delivery of antidiabetic peptides
IN Danley, Dennis Edward; Gelfand, Robert Alan; Geoghegan, Kieran Francis; Yesook, Kim; Lambert, William Joseph; Hong, Qi
PA Pfizer Inc., USA
SO Eur. Pat. Appl., 70 pp.
CODEN: EPXXDW
DT Patent
LA English
IC ICM C07K007-34
ICS C07K007-10; A61K037-28
CC 63-6 (**Pharmaceuticals**)
Section cross-reference(s): 2
FAN.CNT 1

	PATENT NO.	KIND	DATE		APPLICATION NO.	DATE	
PI	EP 619322	A2	19941012		EP 1994-300981	19940210	<--
	EP 619322	A3	19960313				
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE						
	NO 9400436	A	19941010		NO 1994-436	19940209	<--
	AU 9455016	A1	19941013		AU 1994-55016	19940209	<--
	AU 682328	B2	19971002				
	ZA 9400878	A	19950810		ZA 1994-878	19940209	<--
	PL 180697	B1	20010330		PL 1994-302370	19940224	<--
	CA 2116478	AA	19941008		CA 1994-2116478	19940225	<--
	CA 2116478	C	20021203				
	JP 07002695	A2	19950106		JP 1994-35948	19940307	<--
	RU 2126264	C1	19990220		RU 1994-7084	19940307	<--
	JP 2001158749	A2	20010612		JP 2000-317228	19940307	<--
	BR 9401185	A	19941018		BR 1994-1185	19940316	<--
	CN 1106698	A	19950816		CN 1994-104491	19940407	<--
	CN 1080123	B	20020306				
	US 6284727	B1	20010904		US 1995-472349	19950607	<--
	US 2003050237	A1	20030313		US 2001-943084	20010831	<--
PRAI	US 1993-44133	A	19930407	<--			
	US 1994-181655	B1	19940125	<--			
	JP 1994-35948	A3	19940307	<--			
	US 1995-472349	A1	19950607	<--			

AB Noninsulin-dependent diabetes mellitus is treated in a mammal by prolonged administration of peptide 7-37 of **glucagon**-like peptide 1 (insulinotropin, GLP-1) and related peptides, especially in combination with a polymer matrix, in a water-immiscible oil suspension, in a complex with Zn or other metals, in a complex with a basic polypeptide or phenolic compound, in a liposome delivery system, or after subjection to conditions resulting in amorph. or crystalline material formation (e.g. high shear or exposure to salts) to prolong the release of the peptide. Thus, a solution containing 2 mg insulinotropin/mL phosphate-buffered saline (PBS) was mixed with an equal volume of a solution of 0.6 mg protamine and 4.4 mg PhOH/mL in PBS to produce an aqueous suspension.
ST insulinotropin prolonged release; antidiabetic peptide prolonged release
IT Phenols, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combinations with peptides; prolonged delivery of antidiabetic peptides)
IT Polyamides, biological studies
Polyanhydrides
Polyesters, biological studies

Polymers, biological studies
Polysaccharides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(matrixes; prolonged delivery of antidiabetic peptides)

IT Shear
(peptide insolubilization by; prolonged delivery of antidiabetic peptides)

IT Salts, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(peptide insolubilization by; prolonged delivery of antidiabetic peptides)

IT Antidiabetics and Hypoglycemics
(prolonged delivery of antidiabetic peptides)

IT Castor oil
Coconut oil
Corn oil
Cottonseed oil
Fats and Glyceridic oils
Olive oil
Peanut oil
Safflower oil
Soybean oil
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(suspensions; prolonged delivery of antidiabetic peptides)

IT Fats and Glyceridic oils
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(almond, suspensions; prolonged delivery of antidiabetic peptides)

IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(basic, complexes, with peptides; prolonged delivery of antidiabetic peptides)

IT Ortho acids
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(esters, polymers, as matrixes; prolonged delivery of antidiabetic peptides)

IT Fatty acids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(esters, suspensions; prolonged delivery of antidiabetic peptides)

IT Alcohols, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fatty, esters, suspensions; prolonged delivery of antidiabetic peptides)

IT Pharmaceutical dosage forms
(liposomes, prolonged delivery of antidiabetic peptides)

IT Fats and Glyceridic oils
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sesame, suspensions; prolonged delivery of antidiabetic peptides)

IT Protamines
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sulfates, peptide complexes; prolonged delivery of antidiabetic peptides)

IT Fats and Glyceridic oils
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(teaseed, suspensions; prolonged delivery of antidiabetic peptides)

IT 99-76-3, Methyl paraben 108-39-4, biological studies 108-46-3, Resorcinol, biological studies 108-95-2, Phenol, biological studies 1319-77-3, Cresol
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combinations with peptides; prolonged delivery of antidiabetic peptides)

IT 9000-01-5, Gum acacia 9000-07-1, Carrageenan 9000-21-9, Furcellaran 9000-30-0, Guar gum 9000-36-6, Karaya gum 9000-65-1, Gum tragacanth 9002-89-5, PVA 9003-11-6, Ethylene glycol/propylene glycol copolymer

9003-39-8, PVP 9004-34-6, Cellulose, biological studies 9004-34-6D, Cellulose, derivs. 9004-54-0, Dextran, biological studies 9004-61-9, Hyaluronic acid 9004-62-0, Hydroxyethylcellulose 9005-25-8, Starch, biological studies 9005-25-8D, Starch, derivs. 9005-32-7, Alginic acid 9012-36-6, Agarose 9012-76-4, Chitosan 11138-66-2, Xanthan gum 25322-68-3, PEG
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(matrix; prolonged delivery of antidiabetic peptides)

IT 127-09-3, Sodium acetate 141-53-7, Sodium formate 557-34-6, Zinc acetate 631-61-8, Ammonium acetate 994-36-5, Sodium citrate 6484-52-2, Ammonium nitrate, biological studies 7447-40-7, Potassium chloride, biological studies 7447-41-8, Lithium chloride, biological studies 7487-88-9, Magnesium sulfate, biological studies 7632-05-5, Sodium phosphate 7632-50-0, Ammonium citrate 7646-79-9, Cobalt chloride, biological studies 7646-85-7, Zinc chloride, biological studies 7647-14-5, Sodium chloride, biological studies 7757-82-6, Sodium sulfate, biological studies 7758-11-4, Dipotassium hydrogen phosphate 7773-01-5, Manganese chloride 7783-20-2, Ammonium sulfate, biological studies 7786-30-3, Magnesium chloride, biological studies 7786-81-4, Nickel sulfate 10043-52-4, Calcium chloride, biological studies 10377-48-7, Lithium sulfate 12125-02-9, Ammonium chloride, biological studies 16068-46-5, Potassium phosphate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(peptide insolubilization by; prolonged delivery of antidiabetic peptides)

IT 87805-34-3 **106612-94-6**, Insulinotropin 107444-51-9 121181-17-7 123475-27-4 **123475-28-5 127650-06-0**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(prolonged delivery of antidiabetic peptides)

IT 7439-89-6D, Iron, peptide complexes 7439-95-4D, Magnesium, peptide complexes 7439-96-5D, Manganese, peptide complexes 7440-02-0D, Nickel, peptide complexes 7440-09-7D, Potassium, peptide complexes 7440-48-4D, Cobalt, peptide complexes 7440-50-8D, Copper, peptide complexes 7440-66-6D, Zinc, peptide complexes 7440-70-2D, Calcium, peptide complexes
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prolonged delivery of antidiabetic peptides)

L58 ANSWER 21 OF 21 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:580232 HCAPLUS
DN 121:180232
ED Entered STN: 15 Oct 1994
TI Preparation of **glucagon**-like peptide and insulinotropin derivatives for treating type II diabetes.
IN Andrews, Glenn C.; Daumy, Gaston O.; Francoeur, Michael L.; Larson, Eric R.
PA Pfizer Inc., USA
SO PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07K007-34
ICS A61K037-43
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): **1**
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9325579	A1	19931223	WO 1993-US3388	19930414 <--

W: AU, BR, CA, CZ, DE, JP, KR, NO, NZ, PL, RU, SK, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

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     AU 9340275        A1   19940104       AU 1993-40275    19930414 <--
     AU 671117         B2   19960815
     EP 646128         A1   19950405       EP 1993-909505   19930414 <--
        R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE
     JP 07504679       T2   19950525       JP 1993-501448   19930414 <--
     JP 2575298        B2   19970122
     BR 9306551        A    19980915       BR 1993-6551     19930414 <--
     PL 176007         B1   19990331       PL 1993-306766   19930414 <--
     RU 2128663        C1   19990410       RU 1994-46251    19930414 <--
     EP 969016         A2   20000105       EP 1999-110184   19930414 <--
        R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE
     IL 120890         A1   20000831       IL 1993-120890   19930607 <--
     HU 64367          A2   19931228       HU 1993-1739     19930614 <--
     CN 1085913        A    19940427       CN 1993-108718   19930614 <--
     CN 1057098        B    20001004
     NO 9404853        A    19941214       NO 1994-4853     19941214 <--
PRAI US 1992-899073    A1   19920615  <--
     EP 1993-909505    A3   19930414  <--
     WO 1993-US3388    A    19930414  <--
     IL 1993-105928    A3   19930607  <--
OS   MARPAT 121:180232
AB   H2NWCO2H (W = His-Asp-Glu-Phe-Glu-Arg-His-Ala-Glu-Gly-Thr-Phe-Thr-Ser-Asp-
     Val-Ser-Ser-Tyr-Leu-Glu-Gly-Gln-Ala-Ala-Lys-Glu-Phe-Ile-Ala-Trp-Leu-Val-
     Lys-Gly-Arg-Gly, His-Asp-Glu-Phe-Glu-Arg-His-Ala-Glu-Gly-Thr-Phe-Thr-Ser-
     Asp-Val-Ser-Ser-Tyr-Leu-Glu-Gly-Gln-Ala-Ala-Lys-Glu-Phe-Ile-Ala-Trp-Leu-
     Val-Lys-Gly-Arg), and derivs. thereof, having pI ≤4 or ≥7,
     were prepared having insulinotropic activity (no data).  Thus,
     H-His-Ala-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Val-Ser-Ser-Tyr-Leu-Glu-Gly-Gln-Ala-
     Ala-Lys-Glu-Phe-Ile-Ala-Trp-Leu-Val-Lys-Gly-Arg-Gly-Arg-NH2 was prepared by
     solid phase synthesis using BOC-protected amino acids on benzhydrylamine
     resin.  The invention also relates to new uses of certain known derivs. of
     insulinotropin and truncated insulinotropin to enhance insulin action in a
     mammal by iontophoretic administration of such derivs.
ST   insulinotropin deriv prepn diabetes treatment; glucagon like
     peptide antidiabetic; iontophoresis insulinotropin deriv
IT   Iontophoresis
        (administration of glucagon-like peptide and insulinotropin
        derivs by)
IT   Antidiabetics and Hypoglycemics
        (glucagon-like peptide and insulinotropin derivs)
IT   Peptides, preparation
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (preparation of glucagon-like peptide and insulinotropin derivs
        for treatment of type II diabetes)
IT   157507-31-8DP, resin bound
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (preparation of, as intermediate for drug for enhancing insulin action)
IT   87805-34-3P   106612-94-6P   121181-17-7P   123475-27-4P
     123475-28-5P 127650-06-0P   157507-31-8P
     157569-66-9DP, succinoylated   157569-66-9P   157629-57-7P   157629-58-8P
     157629-61-3P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (preparation of, for enhancing insulin action)
IT   108-30-5, reactions   13836-37-8, BOC-Arg(Tos)-OH   15260-10-3,
     BOC-Thr(Bzl)-OH   23680-31-1, BOC-Ser(Bzl)-OH   47355-10-2,
     BOC-Trp(CHO)-OH   47689-67-8, BOC-Tyr(Br-Z)-OH   54613-99-9,
     BOC-Lys(Cl-Z)-OH   73821-95-1, BOC-Asp(OCyHex)-OH   73821-97-3,
     BOC-Glu(OCyHex)-OH   83468-83-1, BOC-His(BOM)-OH
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, in preparation of peptide drug for enhancing insulin action)


=> => d his 158-
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L58          21 S L53,L57

     FILE 'REGISTRY' ENTERED AT 16:31:50 ON 22 JAN 2004

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L59           9 S L34 NOT L58

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L59  ANSWER 1 OF 9  HCAPLUS  COPYRIGHT 2004 ACS on STN
AN   2000:335587  HCAPLUS
DN   133:3760
ED   Entered STN:  19 May 2000
TI   Enzymatic amidation of peptides
IN   Dormady, Dan; Stout, Jay S.; Strydom, Daniel J.; Holmquist, Barton;
     Wagner, Fred W.
PA   Bionebraska, Inc., USA
SO   PCT Int. Appl., 48 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
IC   ICM  C12P021-06
     ICS  C12N009-50; C07K014-605
CC   16-2 (Fermentation and Bioindustrial Chemistry)
     Section cross-reference(s): 34
FAN.CNT 1
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             JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK,
             MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ,
             TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ,
             MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
             DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
             CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     US 6461834          B1    20021008       US 1998-212663   19981216 <--
     EP 1127155          A1    20010829       EP 1999-956920   19991105 <--
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
     JP 2002529101       T2    20020910       JP 2000-581233   19991105 <--
     AU 755130           B2    20021205       AU 2000-13423    19991105 <--
     ZA 2001002694       A     20021002       ZA 2001-2694     20010402 <--
     NO 2001002232       A     20010504       NO 2001-2232     20010504 <--
PRAI US 1998-107311P     P     19981106  <--
     US 1998-212663      A2    19981216  <--
     WO 1999-US26060     W     19991105
AB   The invention provides a method of producing a polypeptide having a
     C-terminal α-carboxamide group.  It particularly concerns an enzymic
     modification of selected substrate polypeptides which result in cleavage
     of the substrate polypeptide to form a product peptide with a C-terminal
     arginine residue having an α-carboxamide group (C-terminal
     "Arg-NH2").  The method includes contacting an aqueous-based solution including
     (i) NH3 reagent and (ii) the substrate polypeptide with (iii) clostripain.
ST   clostripain peptide cleavage amidation
IT   Amidation
        (enzymic amidation of peptides)
IT   Peptides, biological studies
     RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); BPR
```

(Biological process); BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)
(enzymic amidation of peptides)

IT Immobilization, biochemical
(of clostripain for enzymic amidation of peptides)

IT 9028-00-6P, Clostripain
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); CAT (Catalyst use); PEP (Physical, engineering or chemical process); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(enzymic amidation of peptides)

IT 269080-54-8P 269080-55-9P
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(enzymic amidation of peptides)

IT 269080-56-0 269080-57-1 269080-58-2 269080-59-3 269080-60-6
269080-61-7 269080-62-8 269080-63-9 269080-64-0 269080-65-1
269080-66-2 269080-67-3 269080-68-4 269080-69-5 270069-93-7
270069-94-8
RL: BPR (Biological process); BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent)
(enzymic amidation of peptides)

IT 68-12-2, biological studies 75-05-8, Acetonitrile, biological studies 75-89-8 108-32-7, Propylene carbonate 3483-12-3, Dithiothreitol
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(enzymic amidation of peptides)

IT 631-61-8, Ammonium acetate 1336-21-6, Ammonium hydroxide 7783-20-2, Ammonium sulfate, biological studies 12125-02-9, Ammonium chloride, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent)
(of clostripain for enzymic amidation of peptides)

IT 123475-27-4 **127650-06-0** 270056-54-7 270079-01-1
RL: PRP (Properties)
(unclaimed protein sequence; enzymic amidation of peptides)

IT 269731-05-7
RL: PRP (Properties)
(unclaimed sequence; enzymic amidation of peptides)

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Bionebraska Inc; WO 9401451 A 1994 HCAPLUS
(2) Bionebraska Inc; WO 9617941 A 1996 HCAPLUS
(3) Calsberg, A; WO 9520039 A 1995 HCAPLUS
(4) Hoechst Ag; EP 0474212 A 1992 HCAPLUS
(5) Hoechst Ag; EP 0518088 A 1992 HCAPLUS
(6) Kembhavi, A; FEBS LETTERS 1991, V283(2), P277 HCAPLUS
(7) Kernforschungsanlage Juelich; EP 0401657 A 1990 HCAPLUS

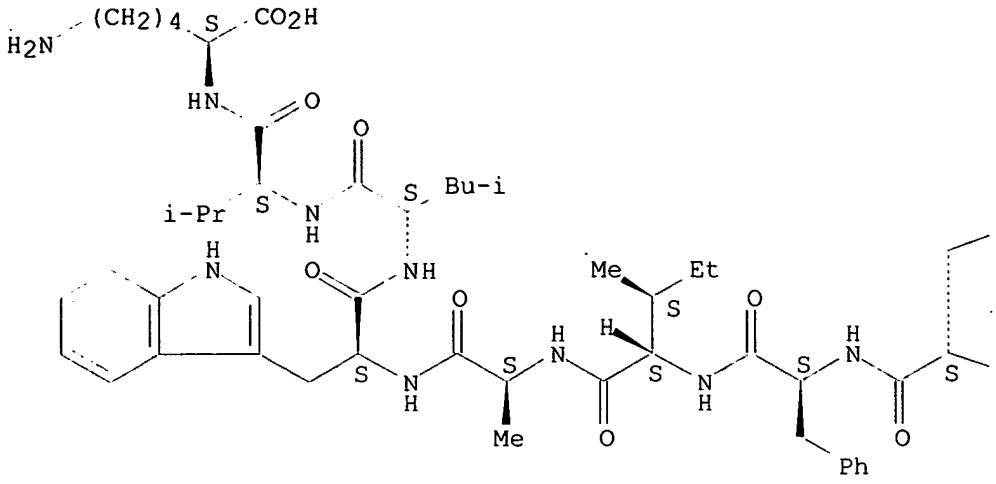
IT **127650-06-0**
RL: PRP (Properties)
(unclaimed protein sequence; enzymic amidation of peptides)

RN 127650-06-0 HCAPLUS

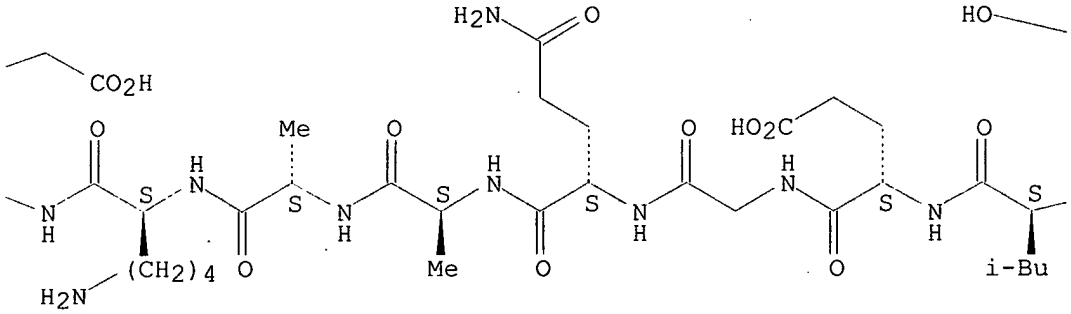
CN L-Lysine, L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



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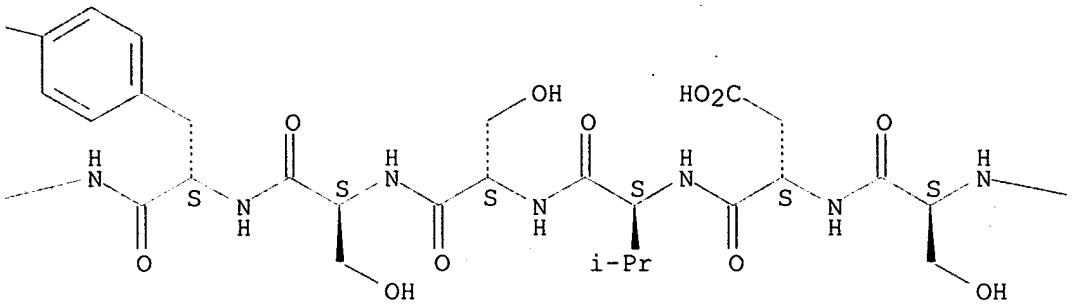

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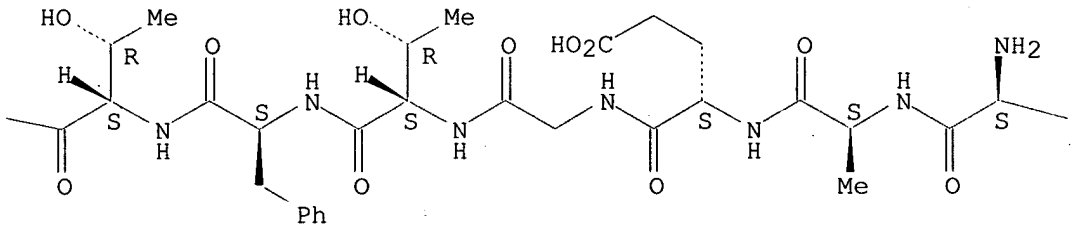

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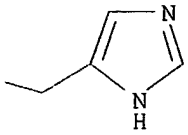

L59 ANSWER 2 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:43882 HCAPLUS
DN 126:127176
ED Entered STN: 20 Jan 1997
TI **Glucagon**-like peptide-1-(9-36) amide is a major metabolite of **glucagon**-like peptide-1-(7-36) amide after in vivo administration to dogs, and it acts as an antagonist on the pancreatic receptor
AU Knudsen, Lotte Bjerre; Pridal, Lone
CS Novo Nordisk, Novo Alle, DK-2880, Bagsvaerd, Den.
SO European Journal of Pharmacology (**1996**), 318(2/3), 429-435
CODEN: EJPHAZ; ISSN: 0014-2999
PB Elsevier
DT Journal
LA English
CC 2-6 (Mammalian Hormones)
AB This study assesses the importance of metabolites formed following exogenous administration of **glucagon**-like peptide-1-(7-36) amide (GLP-1). After s.c. administration of GLP-1 to dogs the plasma immunoreactivity of GLP-1 measured by two different RIAs were higher than that measured by a sandwich ELISA. This discrepancy was due to the formation of the metabolites GLP-1-(9-36) amide, GLP-1-(7-35) and GLP-1-(7-34). Receptor binding studies using baby hamster kidney cells expressing the human pancreatic GLP-1 receptor showed that the affinity of GLP-1-(9-36) amide, GLP-1-(7-35) and GLP-1-(7-34) was 0.95, 12 and 2.8, resp., of the affinity of GLP-1-(7-36) amide. Furthermore, GLP-1-(9-36) amide was shown to be an antagonist to adenylyl cyclase activity, whereas GLP-1-(7-35) and GLP-1-(7-34) were shown to be agonists. GLP-1-(9-36) amide was shown to be present in vivo in amts. up to 10-fold that of GLP-1-(7-36) amide. Due to its low binding affinity, this antagonistic metabolite does not seem to be able to cause physiol. antagonism upon s.c. administration of the peptide.
ST glucagonlike peptide fragment metabolite pancreas receptor
IT Pancreas
(**glucagon**-like peptide-1-(9-36) amide is major metabolite of **glucagon**-like peptide-1-(7-36) amide after in vivo administration to dogs and an antagonist on pancreatic receptor)
IT **Glucagon**-like peptide-1 receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**glucagon**-like peptide-1-(9-36) amide is major metabolite of **glucagon**-like peptide-1-(7-36) amide after in vivo administration to dogs and an antagonist on pancreatic receptor)
IT 161748-29-4

RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence)
(**glucagon**-like peptide-1-(9-36) amide is major metabolite of **glucagon**-like peptide-1-(7-36) amide after in vivo administration to dogs and an antagonist on pancreatic receptor)

IT 118549-37-4, Insulinotropin
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**glucagon**-like peptide-1-(9-36) amide is major metabolite of **glucagon**-like peptide-1-(7-36) amide after in vivo administration to dogs and an antagonist on pancreatic receptor)

IT **123475-28-5 127650-06-0**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(**glucagon**-like peptide-1-(9-36) amide is major metabolite of **glucagon**-like peptide-1-(7-36) amide after in vivo administration to dogs and an antagonist on pancreatic receptor)

IT 9012-42-4, Adenylyl cyclase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**glucagon**-like peptide-1-(9-36) amide is major metabolite of **glucagon**-like peptide-1-(7-36) amide after in vivo administration to dogs and an antagonist on pancreatic receptor)

RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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(2) Cottrell, D; Clin Res 1992, V40, P734A
(3) Deacon, C; Diabetes 1995, V44, P1126 HCAPLUS
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(9) Gallwitz, B; Eur J Biochem 1994, V225, P1151 HCAPLUS
(10) Gefel, D; Endocrinology 1990, V126, P2164 HCAPLUS
(11) Grandt, D; Digestion 1994, V55, P302
(12) Gutniak, M; New Engl J Med 1992, V326, P1316 MEDLINE
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(25) Unson, C; Proc Natl Acad Sci USA 1987, V84, P4083 HCAPLUS

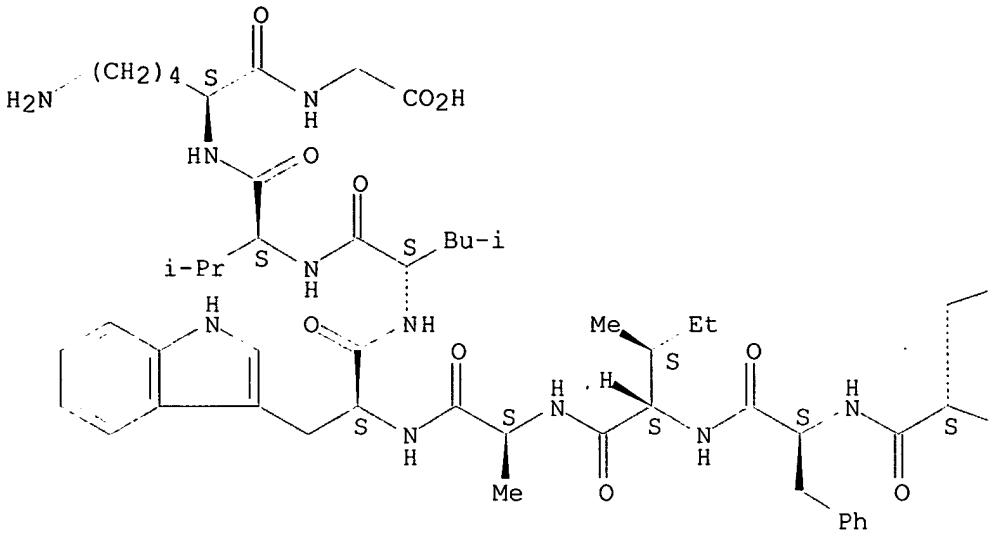
IT **123475-28-5 127650-06-0**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(**glucagon**-like peptide-1-(9-36) amide is major metabolite of **glucagon**-like peptide-1-(7-36) amide after in vivo administration to dogs and an antagonist on pancreatic receptor)

RN 123475-28-5 HCAPLUS
CN Glycine, L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-

phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-lysyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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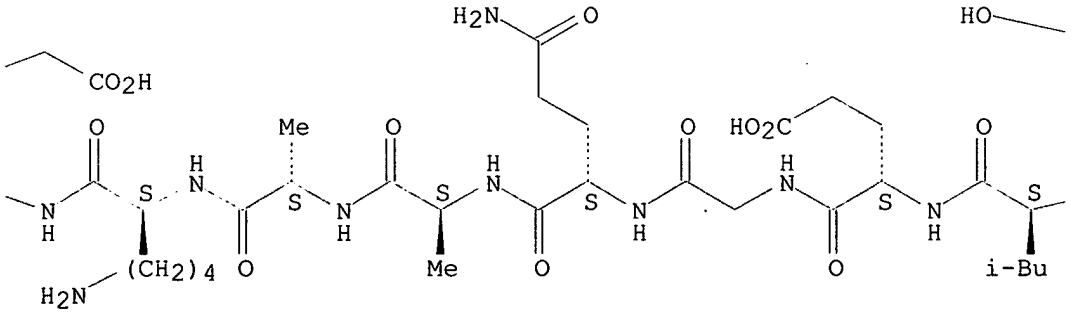

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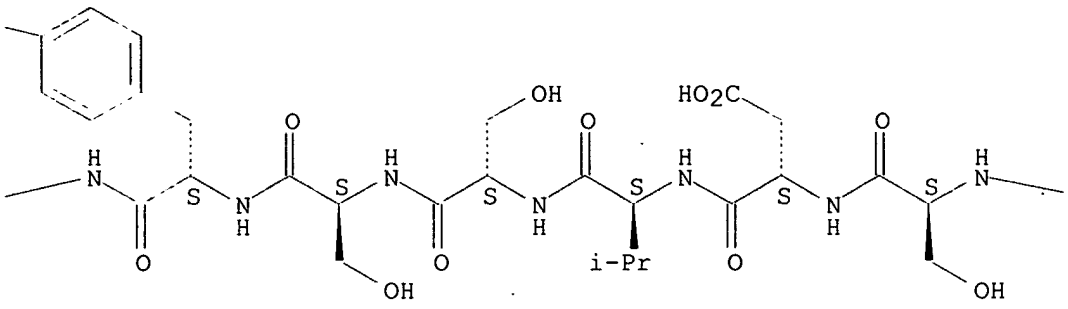

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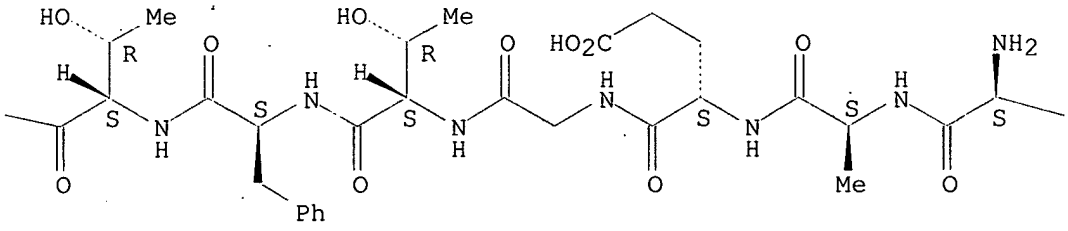

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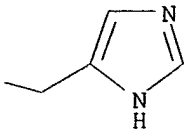
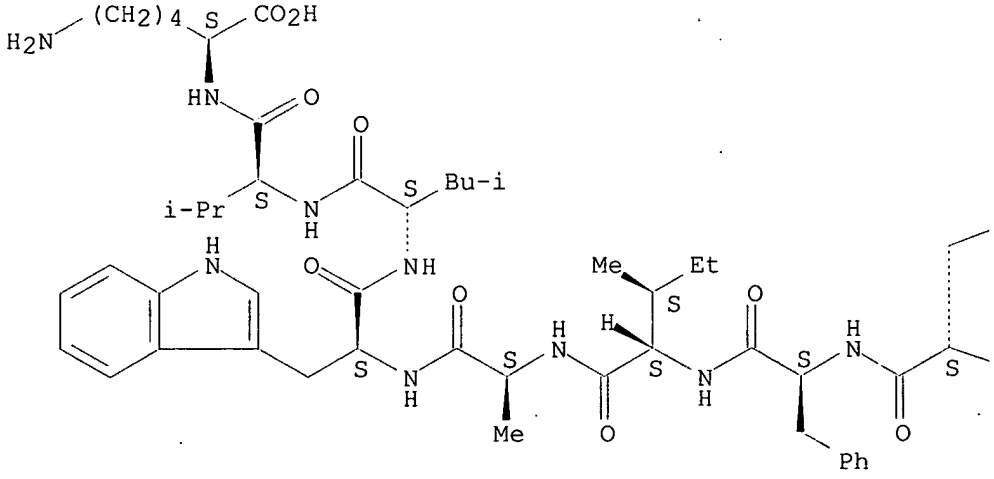


RN 127650-06-0 HCAPLUS
CN L-Lysine, L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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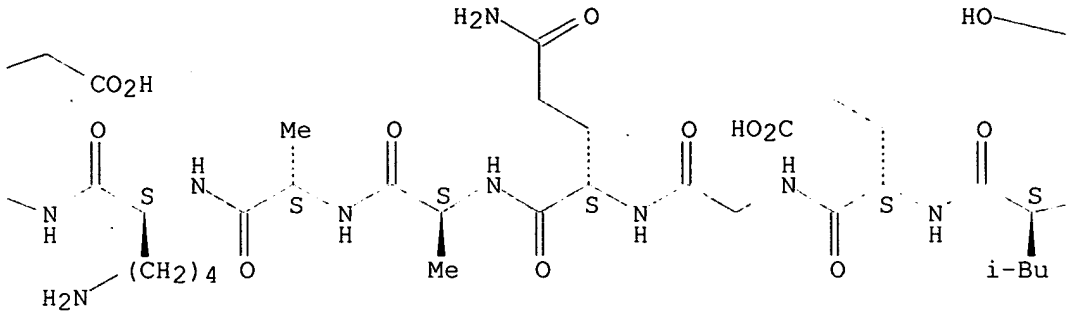

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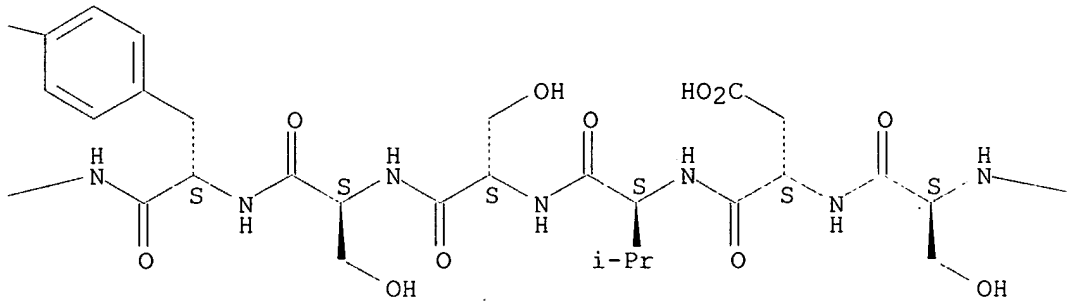

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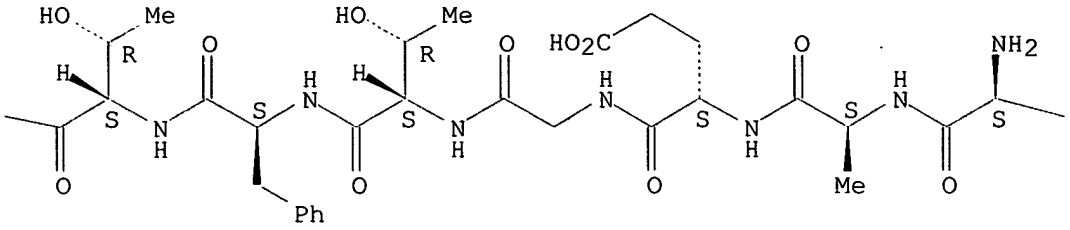

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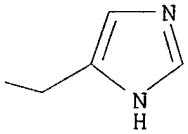


L59 ANSWER 3 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1993:94498 HCAPLUS
DN 118:94498
ED Entered STN: 19 Mar 1993
TI Structural requirements for biological activity of **glucagon**-like peptide-I
AU Moisov, Svetlana
CS Rockefeller Univ., New York, NY, USA
SO International Journal of Peptide & Protein Research (**1992**), 40(3-4), 333-43
CODEN: IJPPC3; ISSN: 0367-8377
DT Journal
LA English
CC 2-2 (Mammalian Hormones)
Section cross-reference(s): 34
AB **Glucagon**-like peptide-I (GLP-I) is encoded together with **glucagon** by the **glucagon** gene and is related in its structure to the **glucagon**-secretin family of peptides. Three of the predicted forms of the peptide, a 37-residue long GLP-I(1-37), a 31-residue GLP-I(7-37) and a 30-residue GLP-I(7-36) amide as well as 3

analogs des[Gly37,Arg36]GLP-I(7-37), des[Gly37,Arg36,Gly35]GLP-I(7-37) and des[His7]GLP-I(7-37) were synthesized by the stepwise solid-phase method. These synthetic peptides were used to define the structural domains required for the binding of GLP-I to the pancreatic β-cell. The competitive binding expts. showed that both the amino and carboxyl terminal domains of the mol. contribute to GLP-I binding. In these expts. **glucagon**, another peptide that stimulates insulin secretion, was a weak full agonist of GLP-I binding. Results from these studies provide further characterization of the physiol. role of this new peptide.

ST **glucagon** like peptide structure activity; peptide prepn **glucagon** like

IT Receptors
RL: BIOL (Biological study)
(**glucagon**-related peptide I, of pancreatic islet β-cell, ligand binding by, structure in relation to)

IT Molecular structure-biological activity relationship
(receptor-binding, of **glucagon**-like peptide I analogs)

IT Pancreatic islet of Langerhans
(β-cell, **glucagon**-like peptide I receptors of, ligand binding by, structure in relation to)

IT 87805-34-3P, Rat GLP-I(1-37) 106612-94-6P, Rat GLP-I(7-37) 107444-51-9P, Rat GLP-I(7-36)amide **123475-28-5P** 127633-64-1P **127650-06-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and pancreatic islet receptor binding of, structure in relation to)

IT **89750-14-1**, **Glucagon**-like peptide I
RL: BIOL (Biological study)
(receptor for, of pancreatic islet β-cell)

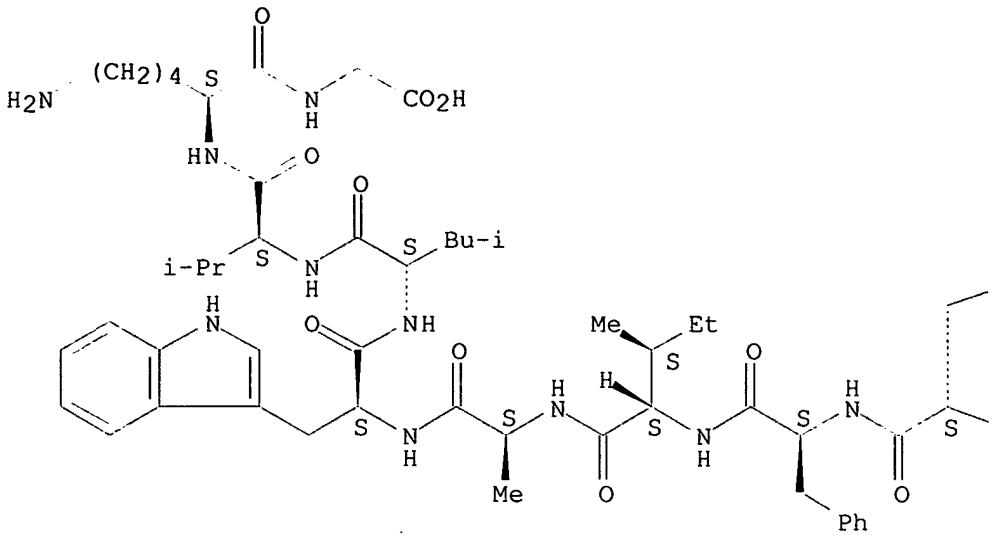
IT **123475-28-5P** **127650-06-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and pancreatic islet receptor binding of, structure in relation to)

RN 123475-28-5 HCAPLUS

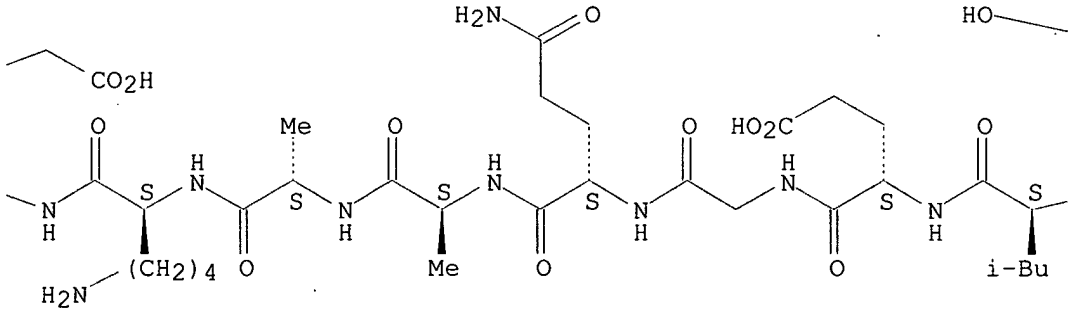
CN Glycine, L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-lysyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



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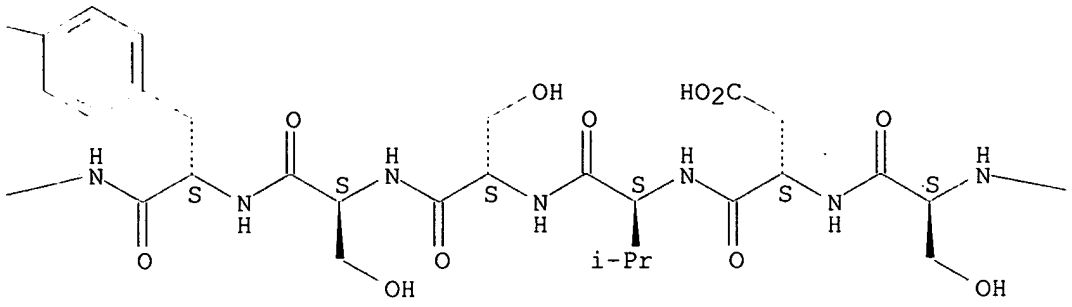

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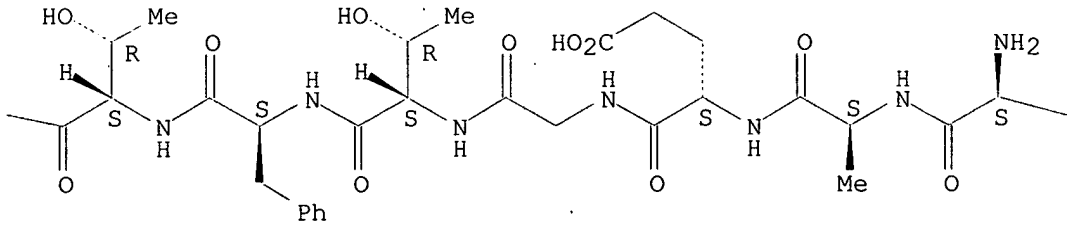

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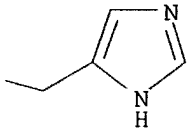
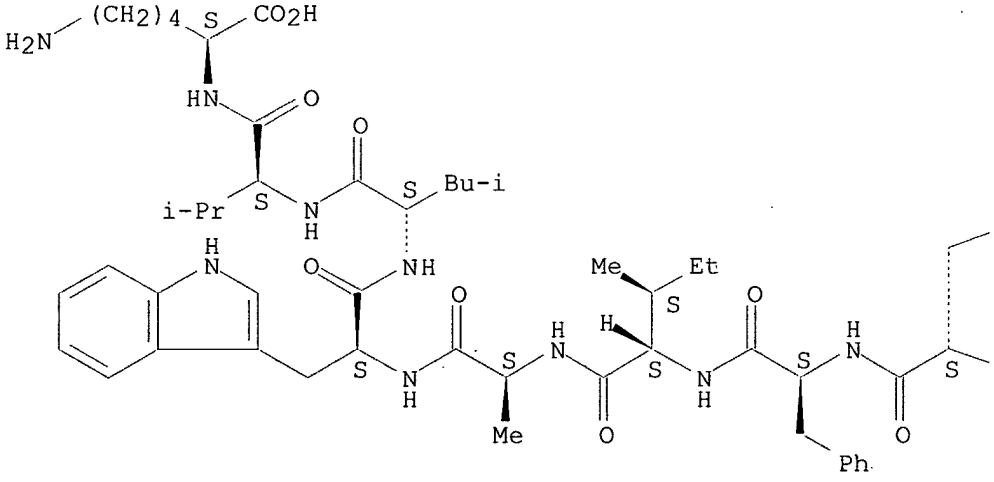


RN 127650-06-0 HCAPLUS
CN L-Lysine, L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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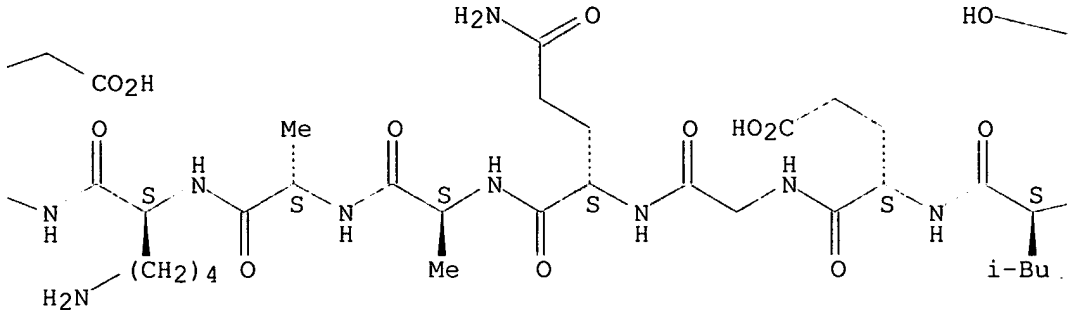

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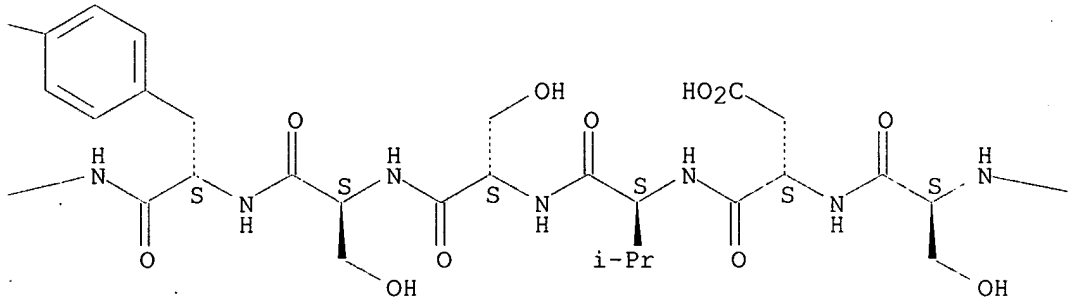
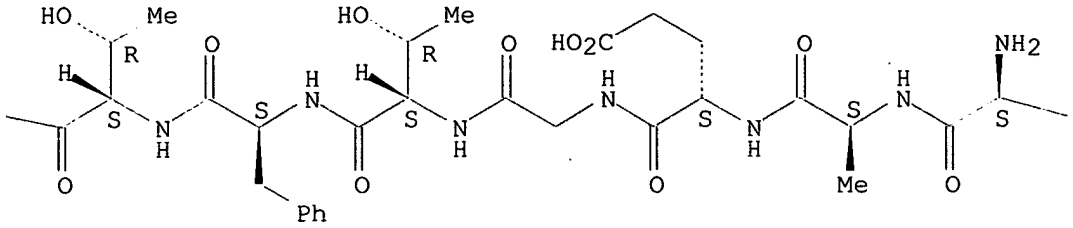
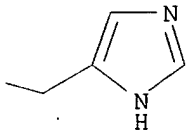


PAGE 1-D



PAGE 1-E



IT **89750-14-1, Glucagon**-like peptide I
RL: BIOL (Biological study)
(receptor for, of pancreatic islet β-cell)
RN 89750-14-1 HCAPLUS
CN Glucagon-like peptide I (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L59 ANSWER 4 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1992:35159 HCAPLUS
DN 116:35159
ED Entered STN: 08 Feb 1992
TI **Glucagon**-like peptide-1 (Glp-1) analogs useful for diabetes treatment
IN Buckley, Douglas I.; Habener, Joel F.; Mallory, Joanne B.; Mojsov, Svetlana
PA USA
SO PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DT Patent
LA English

IC ICM C07K007-34
ICS C07K007-10; A61K037-02; A61K037-28
CC 2-6 (Mammalian Hormones)
FAN.CNT 1

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	CA 2073856	C	20021203				
	EP 512042	A1	19921111		EP 1991-903738	19910124	<--
	EP 512042	B1	19980408				
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE						
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	US 1991-762768	A1	19910920	<--			

AB The invention provides effective analogs of the active GLP-1 peptides, 7-34, 7-35, 7-36, and 7-37, which have improved characteristics for treatment of diabetes Type II. These analogs have amino acid substitutions at positions 7-10 and/or are truncated at the C-terminus and/or contain various other amino acid substitutions in the basic peptide. The analogs may either have an enhanced capacity to stimulate insulin production as compared to **glucagon** or may exhibit enhanced stability in plasma as compared to GLP-1 (7-37) or both. Either of these properties will enhance the potency of the analog as a therapeutic. Analogs having D-amino acid substitutions in the 7 and 8 positions and/or N-alkylated or N-acylated amino acids in the 7 position are particularly resistant to degradation in vivo. Activity and stability data for selected peptides are included.

ST **glucagon** like peptide analog diabetes
IT Antidiabetics and Hypoglycemics
(**glucagon**-like peptide-1 analogs as, for type II diabetes treatment)
IT Peptides, biological studies
RL: BIOL (Biological study)
(**glucagon**-like peptide-2 analogs, for type II diabetes treatment)
IT Molecular structure-biological activity relationship
(of **glucagon**-like peptide-1 analogs, insulin stimulation and diabetes type II treatment in relation to)
IT Protein sequences
(of **glucagon**-like peptide-2 analogs)
IT 106612-94-6 107444-51-9 119637-73-9 123475-27-4 **123475-28-5**
127650-06-0 138324-89-7 138324-90-0 138324-91-1
138324-92-2 138324-93-3 138324-94-4 138324-95-5 138324-96-6
138324-97-7 138324-98-8 138324-99-9 138325-00-5 138347-75-8
138347-76-9
RL: BIOL (Biological study)
(for diabetes type II treatment)
IT 138347-77-0
RL: BIOL (Biological study)
(**glucagon**-like peptide-1 analogs stability in relation to)
IT 138325-01-6

RL: BIOL (Biological study)
(insulin-stimulating activity of, diabetes type II treatment in relation to)

IT 9004-10-8, Insulin, biological studies
RL: BIOL (Biological study)
(stimulation of, **glucagon**-like peptide-1 analogs for, for diabetes type II treatment)

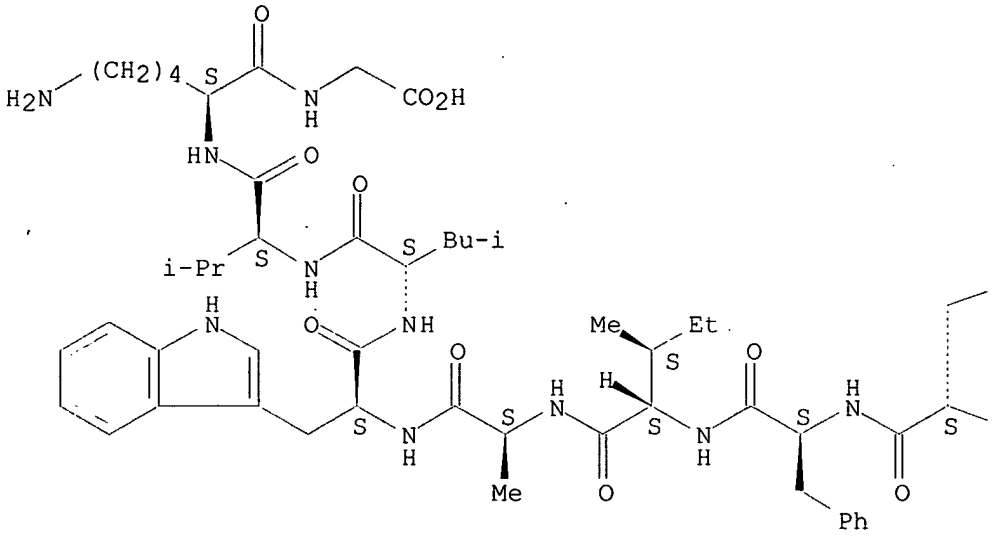
IT **123475-28-5 127650-06-0**
RL: BIOL (Biological study)
(for diabetes type II treatment)

RN 123475-28-5 HCAPLUS

CN Glycine, L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-lysyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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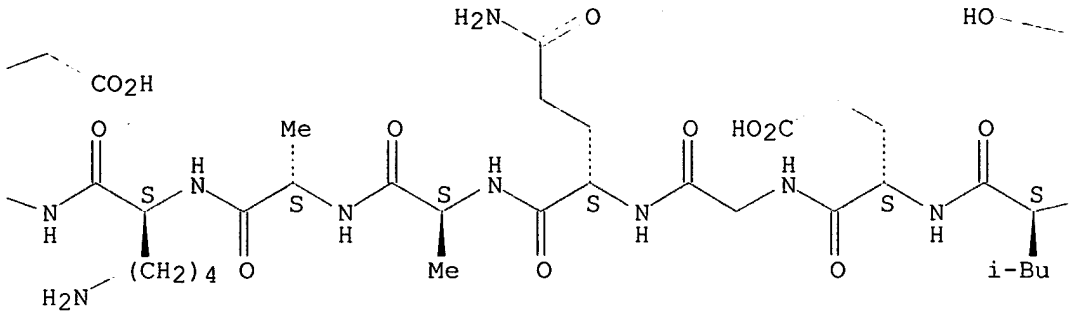

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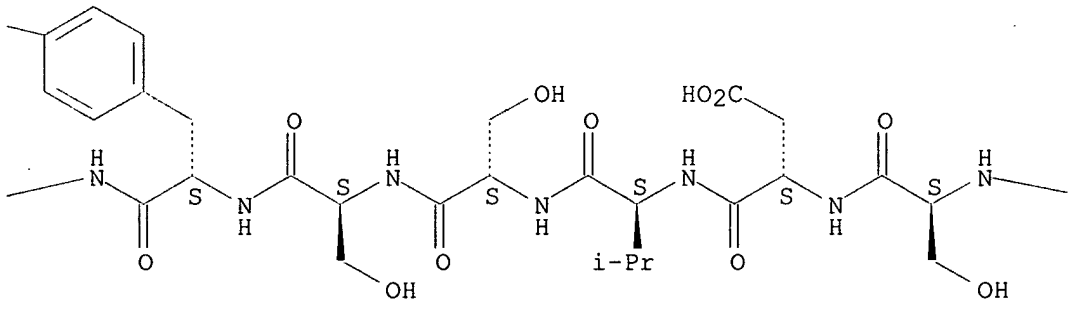

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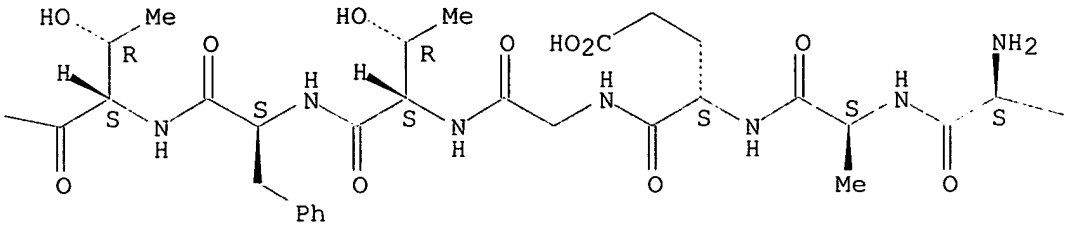
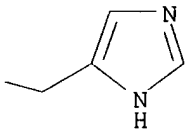


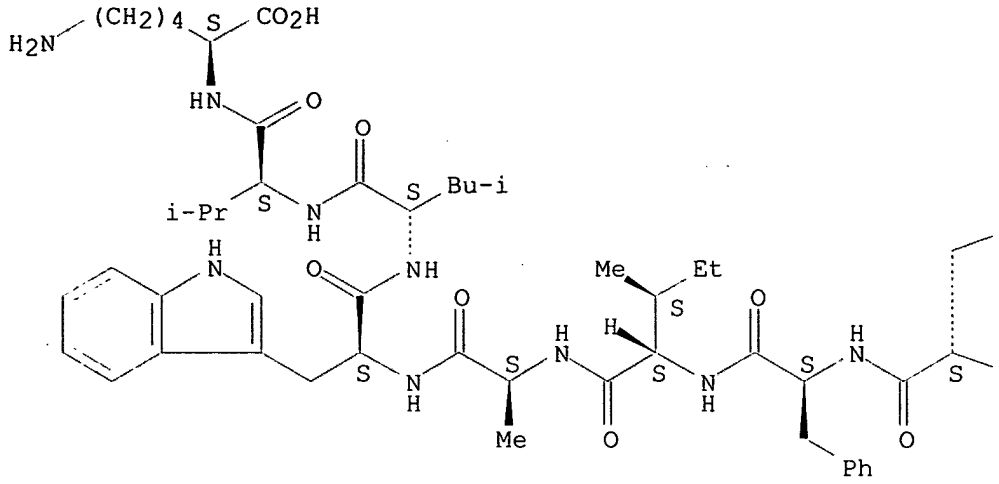
PAGE 1-E



RN 127650-06-0 HCAPLUS
CN L-Lysine, L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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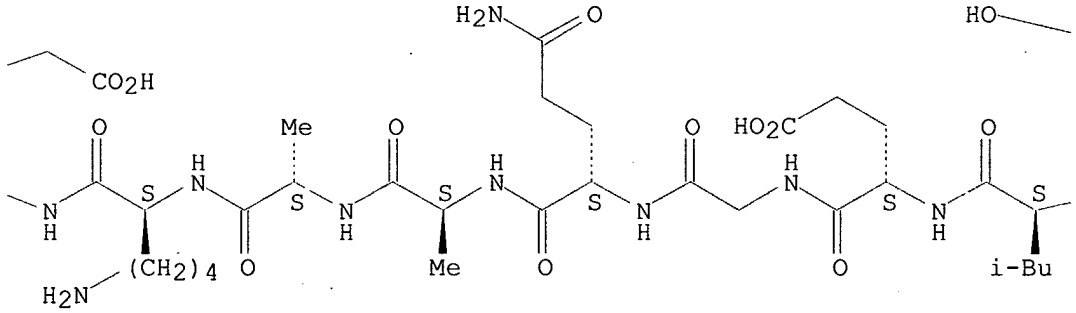

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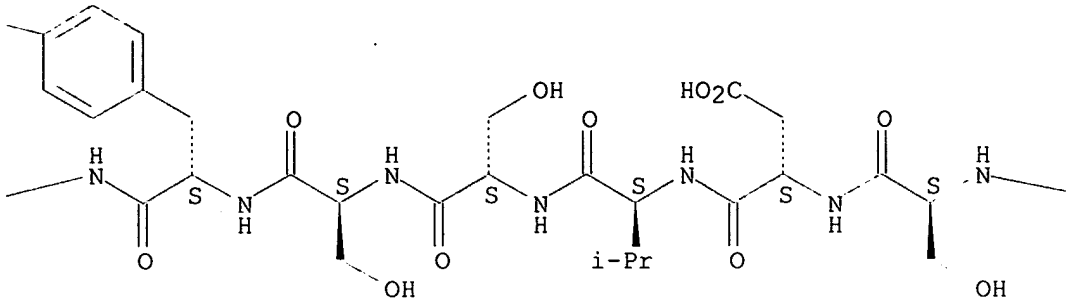

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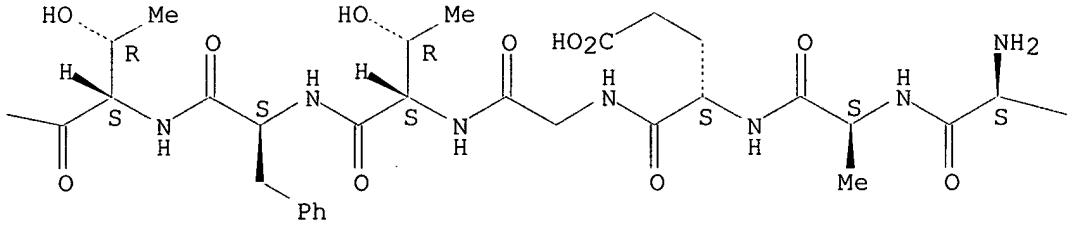

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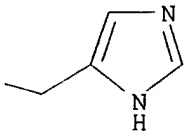
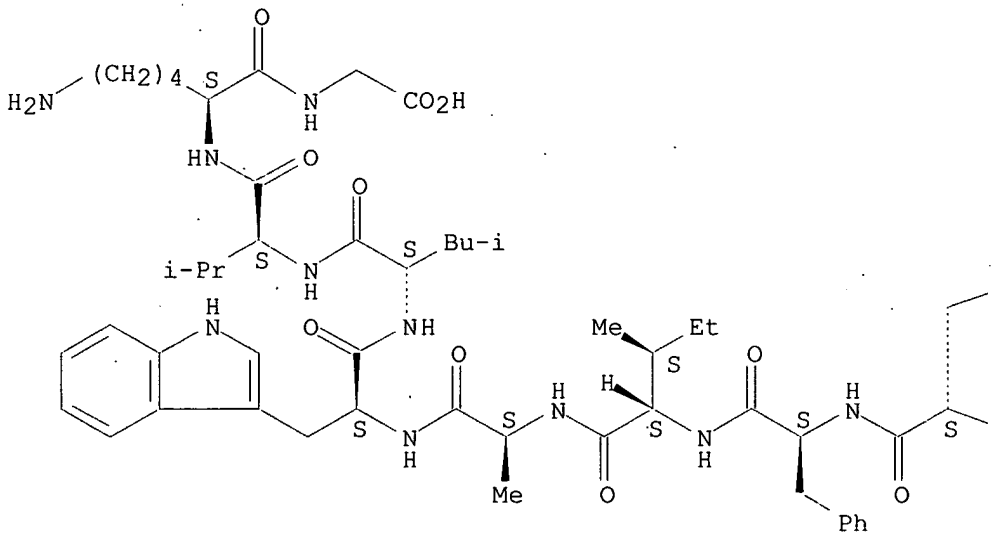


L59 ANSWER 5 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1991:527780 HCAPLUS
DN 115:127780
ED Entered STN: 05 Oct 1991
TI Effects of truncated **glucagon**-like peptide-1 on pancreatic hormone release in normal conscious dogs
AU Kawai, Koichi; Suzuki, Seiji; Ohashi, Shinichi; Mukai, Hidehito; Murayma, Yasuko; Yamashita, Kamejiro
CS Inst. Clin. Med., Univ. Tsukuba, Tsukuba, 305, Japan
SO Acta Endocrinologica (**1990**), 123(6), 661-7
CODEN: ACENA7; ISSN: 0001-5598
DT Journal
LA English
CC 2-6 (Mammalian Hormones)
AB The effects of truncated **glucagon**-like peptide-1 (GLP-1) on insulin and **glucagon** release were examined in unanesthetized normal dogs. A bolus injection of GLP-1(7-36)amide elicited a transient increase in the plasma insulin level, which brought about a decrease in the plasma glucose level. The degree of increase in plasma insulin levels with GLP-1(7-35)OH or GLP-1(7-37)OH was less than that induced by GLP-1(7-36)amide. The plasma **glucagon** level did not increase in spite of mild hypoglycemia. The infusion of graded doses of GLP-1(7-36)amide (6, 36, 120 ng/kg/min every 30 min) did not change the plasma glucose, insulin or **glucagon** levels significantly. The degree of increase in the plasma glucose level induced by i.v. glucose infusion (12 mg/kg/min) was reduced by coinfusion of GLP-1(7-36)amide (6 ng/kg/min), although the degree of increase in the plasma insulin level was the same as that in a control experiment (coinfusion of the vehicle). Coinfusion of GLP-1(7-36)amide (60 ng/kg/min) caused an augmented increase in the plasma insulin level and a reduced increase in the plasma glucose level during i.v. glucose infusion (17 mg/kg/min) compared with the control experiment The degree of decrease in the plasma **glucagon** level during i.v. glucose infusion was not affected by the coinfusion. The degree of increase in the plasma **glucagon** level induced by insulin hypoglycemia and the profile of the plasma glucose level at that time were not affected by the infusion of GLP-1(7-36)amide. These results demonstrate that the insulinotropic activity of GLP-1(7-36)amide is higher than that of GLP-1(7-37)OH or GLP-1(7-35)OH, GLP-1(7-36)amide suppresses the degree of increase in plasma glucose level during i.v. glucose infusion by augmented insulin release, and the glucagonostatic activity of truncated GLP-1 is negligible under physiol. conditions.
ST truncated glucagonlike peptide pancreas hormone; insulinotropin pancreas insulin **glucagon**

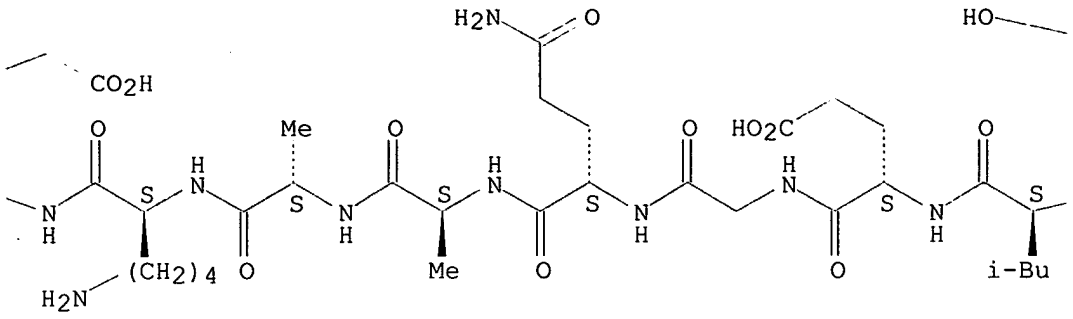
IT 107444-51-9 116964-93-3 118549-37-4, Insulinotropin
123475-28-5 135995-72-1
RL: BIOL (Biological study)
(**glucagon** and insulin secretion response to)
IT 50-99-7, Glucose, biological studies
RL: BIOL (Biological study)
(insulin release response to, truncated **glucagon**-like peptide-1 effect on)
IT 9004-10-8, Insulin, biological studies 9007-92-5, **Glucagon**, biological studies
RL: BIOL (Biological study)
(secretion of, truncated **glucagon**-like peptide-1 effect on)
IT **123475-28-5**
RL: BIOL (Biological study)
(**glucagon** and insulin secretion response to)
RN 123475-28-5 HCAPLUS
CN Glycine, L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-lysyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



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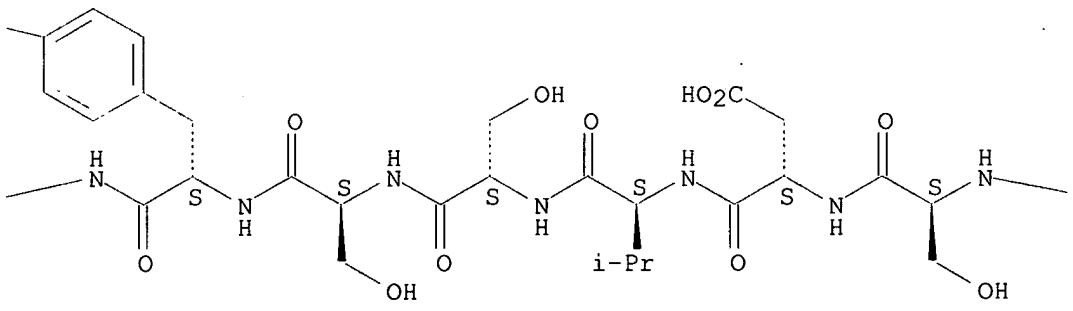

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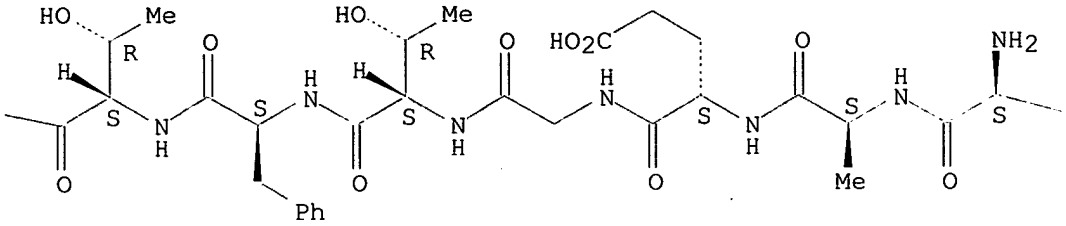

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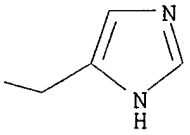


L59 ANSWER 6 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1990:417962 HCAPLUS
DN 113:17962
ED Entered STN: 21 Jul 1990
TI **Glucagon**-like peptide-I analogs: effects on insulin secretion and adenosine 3',5'-monophosphate formation
AU Gefel, Dov; Hendrick, Grant K.; Mojsov, Svetlana; Habener, Joel; Weir, Gordon C.
CS Joslin Diabetes Cent., Boston, MA, 02215, USA
SO Endocrinology (**1990**), 126(4), 2164-8
CODEN: ENDOAO; ISSN: 0013-7227
DT Journal
LA English
CC 2-2 (Mammalian Hormones)
AB **Glucagon**-like peptide I-(7-37) [GLP-I-(7-37)], a 31-amino acid

hormone which may have an important role in the regulation of insulin secretion, is processed from preproglucagon and found in the pancreas, brain, and intestine. It was previously reported that GLP-I-(7-37) is a potent insulin secretagogue, its effect being indistinguishable from that of GLP-I-(7-36) amide at concns. of 10-11 M. Insulinotropic effects of addnl. GLP-I analogs are reported. GLP-I-(7-34) had no stimulatory effect on insulin release at 10-10 M, but had a partial effect at 10-9 M and was as active as GLP-I-(7-37) at 10-8 M. GLP-I-(7-33) had no effect at any concentration tested. GLP-I-(8-37) had no effect on insulin release at 10-9 and 10-8 M, but did have an effect at the high concentration of 10-7 M. Similar results were found with cAMP formation in the βTC1 line. In this system, GLP-I-(7-34) was less potent that GLP-I-(7-37) at a concentration of 5 + 10-9 M. GLP-I-(7-33) had only about 0.1% the potency of GLP-I-(7-37); thus, there is good agreement between cAMP formation in the β-cell line and insulin secretion from the perfused pancreas expts. Histidine in the 7 position in the N-terminus of GLP-I-(7-37) is apparently crucial for cAMP formation and insulin secretion, and removal of the last three C-terminus residues of GLP-I-(7-37) results in only partial loss of activity; the residue in the 34 position is, however, essential for the insulinotropic action.

ST glucagonlike peptide analog insulin cAMP; insulinotropin structure activity

IT Molecular structure-biological activity relationship
(cAMP formation-stimulating, of **glucagon**-like peptide I analogs)

IT Molecular structure-biological activity relationship
(insulin-releasing, of **glucagon**-like peptide I analogs)

IT **89750-14-1D**, **Glucagon**-like peptide I, analogs
106612-94-6, **Glucagon**-like peptide I(7-37) 123475-29-6, **Glucagon**-like peptide I(7-33) 127633-64-1, **Glucagon**-like peptide I(8-37) **127650-06-0**, **Glucagon**-like peptide I(7-34)
RL: BIOL (Biological study)
(cAMP formation and insulin secretion response to)

IT 107444-51-9, **Glucagon**-like peptide I(7-36) amide
123475-28-5, **Glucagon**-like peptide I(7-35)
RL: BIOL (Biological study)
(cAMP formation response to)

IT 60-92-4
RL: FORM (Formation, nonpreparative)
(formation of, by insulinoma cell line, **glucagon**-like peptide I analogs effect on)

IT 9004-10-8, Insulin, biological studies
RL: BIOL (Biological study)
(secretion of, by insulinoma cell line, **glucagon**-like peptide I analogs effect on)

IT **89750-14-1D**, **Glucagon**-like peptide I, analogs
127650-06-0, **Glucagon**-like peptide I(7-34)
RL: BIOL (Biological study)
(cAMP formation and insulin secretion response to)

RN 89750-14-1 HCAPLUS

CN Glucagon-like peptide I (9CI) (CA INDEX NAME)

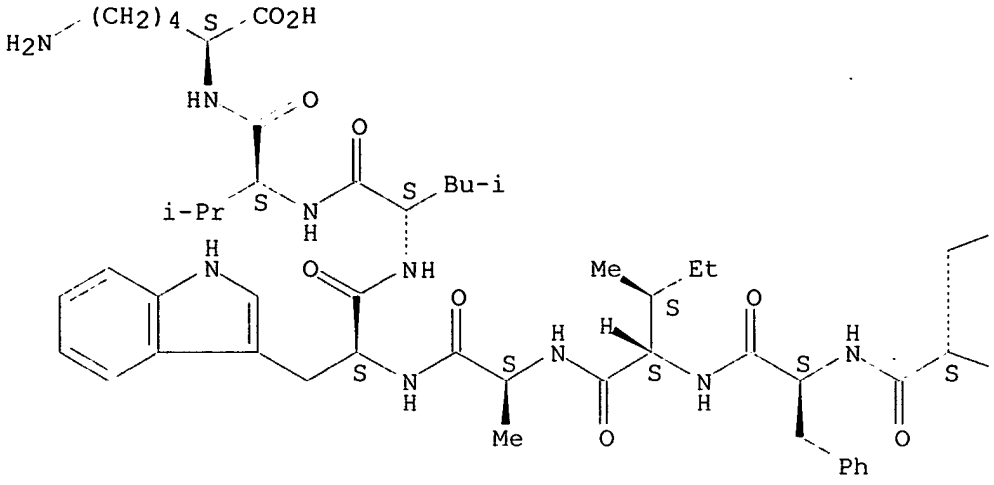
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 127650-06-0 HCAPLUS

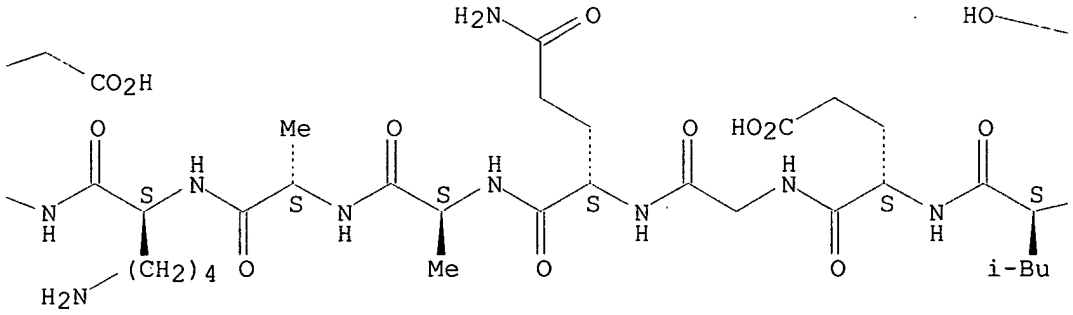
CN L-Lysine, L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

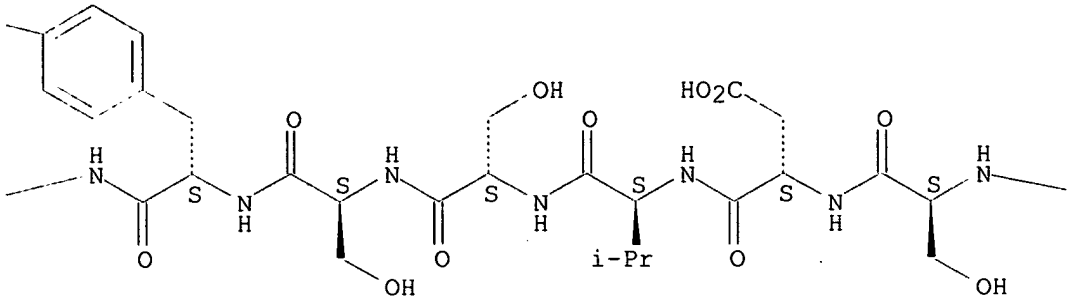
PAGE 1-A



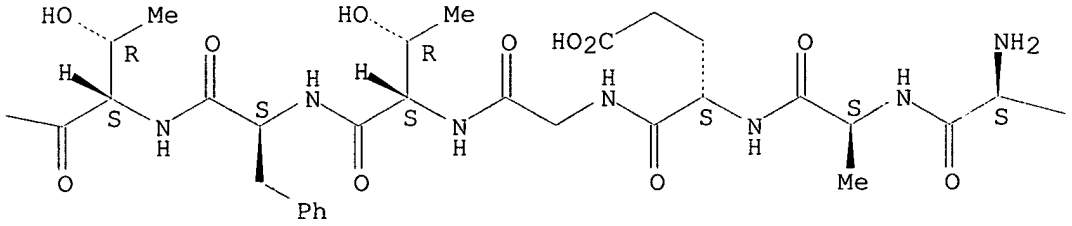
PAGE 1-B



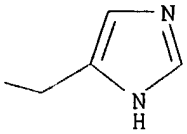
PAGE 1-C



PAGE 1-D



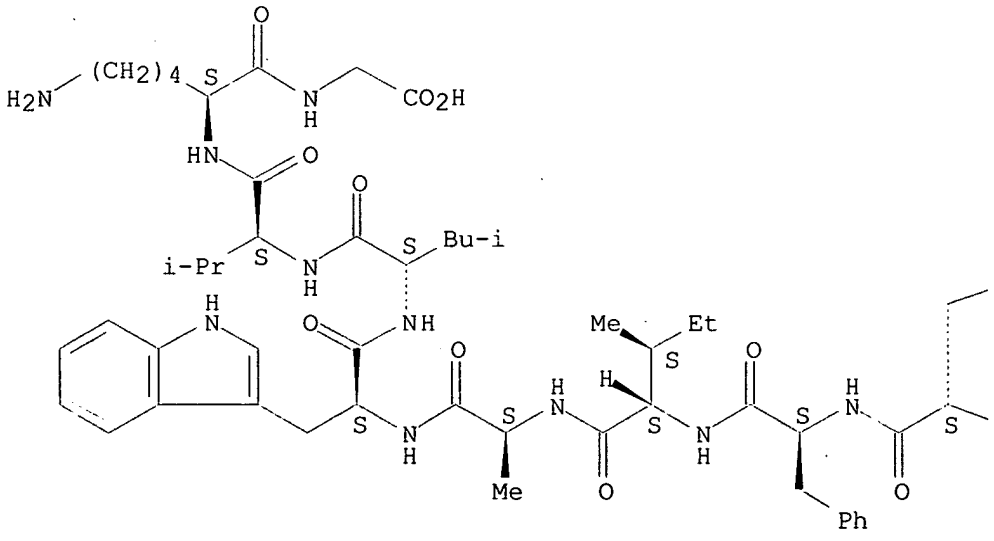
PAGE 1-E



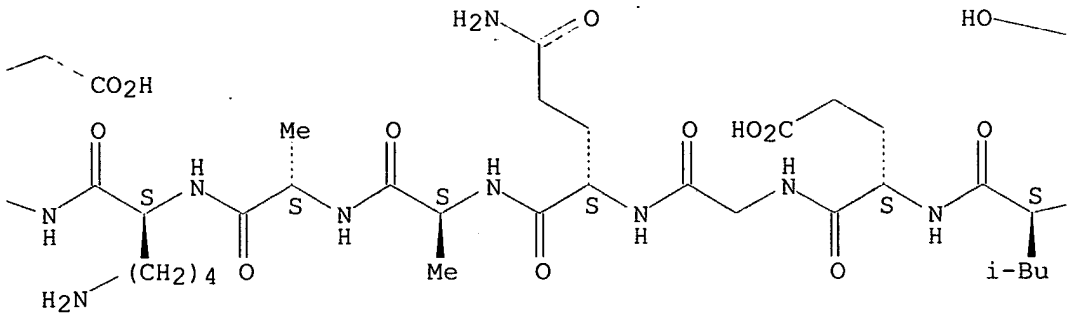
IT **123475-28-5, Glucagon**-like peptide I(7-35)
RL: BIOL (Biological study)
(cAMP formation response to)
RN 123475-28-5 HCAPLUS
CN Glycine, L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-lysyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

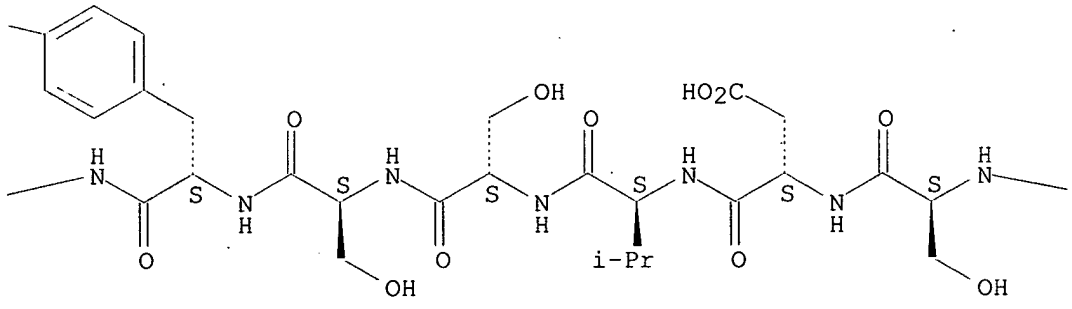
PAGE 1-A



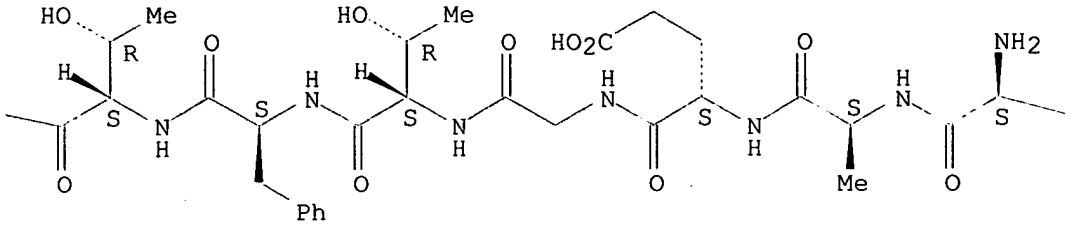
PAGE 1-B



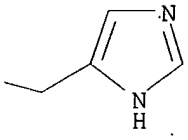
PAGE 1-C



PAGE 1-D



PAGE 1-E



L59 ANSWER 7 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1990:91914 HCAPLUS
DN 112:91914
ED Entered STN: 18 Mar 1990
TI Comparison of the effects of various C-terminal and N-terminal fragment peptides of **glucagon**-like peptide-1 on insulin and **glucagon** release from the isolated perfused rat pancreas
AU Suzuki, Seiji; Kawai, Koichi; Ohashi, Shinichi; Mukai, Hidehito; Yamashita, Kamejiro
CS Inst. Clin. Med., Univ. Tsukuba, Tsukuba, 305, Japan
SO Endocrinology (**1989**), 125(6), 3109-14
CODEN: ENDOAO; ISSN: 0013-7227
DT Journal
LA English
CC 2-2 (Mammalian Hormones)

AB Truncated **glucagon**-like peptide-1 (GLP-1) possesses a potent stimulatory activity for insulin secretion and a slight inhibiting activity for **glucagon** secretion. The activities of N- and C-terminal fragments of GLP-1 were examined using a rat pancreas perfusion system. Concerning the N-terminal portion, GLP-1(7-37) amide elicited a clear insulinotropic activity at 0.1 or 1 nM with the perfusate containing 5.5 mM glucose and 5 mM arginine, while 10 nM GLP-1-(1-37) amide, -(6-37) amide, and -(8-37) amide did not. Concerning the C-terminal portion, GLP-1-(7-37) amide, -(7-37), and -(7-36) amide had a similar potency of insulinotropic activity, and GLP-1-(7-35) was less potent; 0.1 nM GLP-1-(7-35) did not stimulate insulin release, nor did 10 nM GLP-1-(7-20). **Glucagon** release was suppressed by 1 and 10 nM GLP-1-(7-37) amide, 10 nM GLP-1-(7-37), and 1 nM GLP-1-(7-36) amide. Other fragment peptides of GLP-1, including GLP-1-(7-35), had no effect. Apparently, histidine at position 7 of GLP-1 as a free N-terminal amino acid is very important in GLP-1's insulinotropic activity and probably in **glucagon**-inhibiting activity, and C-terminal amidation and the 3 C-terminal amino acids are less important for these activities.

ST glucagonlike peptide 1 insulin release structure; **glucagon** release glucagonlike peptide 1 structure; insulin **glucagon** glucagonlike peptide 1 fragment; structure activity **glucagon** like peptide 1

IT Molecular structure-biological activity relationship
(**glucagon**-releasing, of **glucagon**-like peptide-1 C- and N-terminal fragments)

IT Molecular structure-biological activity relationship
(insulin-releasing, of **glucagon**-like peptide-1 C- and N-terminal fragments)

IT **89750-14-1D**, **Glucagon**-related peptide I, fragments
RL: BIOL (Biological study)
(C- and N-terminal, **glucagon** and insulin release response to, structure in relation to)

IT 87805-34-3, **Glucagon**-related peptide I (ox) 107444-51-9
116964-93-3, **Glucagon**-like peptide-1 (7-37) 119637-73-9
123475-28-5 123496-86-6 123496-87-7 125316-61-2
RL: BIOL (Biological study)
(**glucagon** and insulin release response to, structure in relation to)

IT 9004-10-8, Insulin, biological studies 9007-92-5, **Glucagon**, biological studies
RL: BIOL (Biological study)
(release of, **glucagon**-like peptide-1 C- and N-terminal fragments effect on, structure in relation to)

IT **89750-14-1D**, **Glucagon**-related peptide I, fragments
RL: BIOL (Biological study)
(C- and N-terminal, **glucagon** and insulin release response to, structure in relation to)

RN 89750-14-1 HCAPLUS

CN Glucagon-like peptide I (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

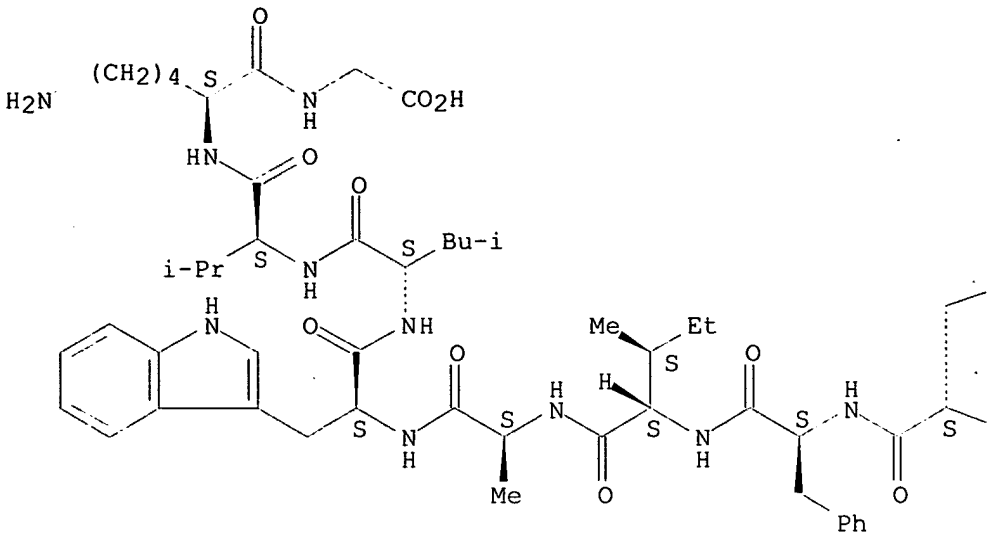
IT **123475-28-5**
RL: BIOL (Biological study)
(**glucagon** and insulin release response to, structure in relation to)

RN 123475-28-5 HCAPLUS

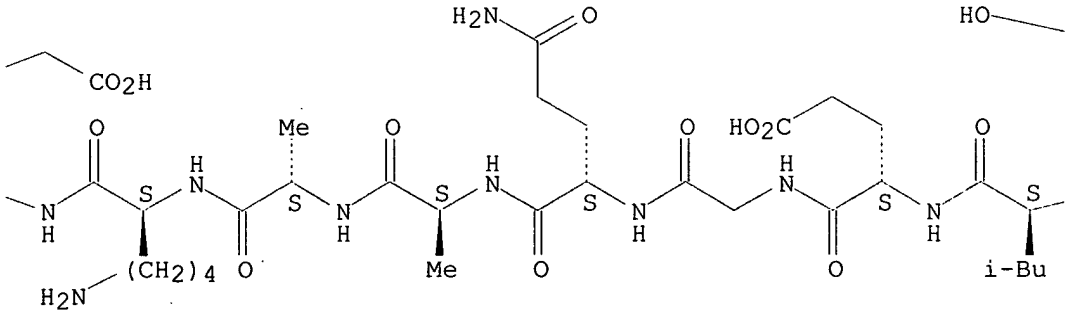
CN Glycine, L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-lysyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

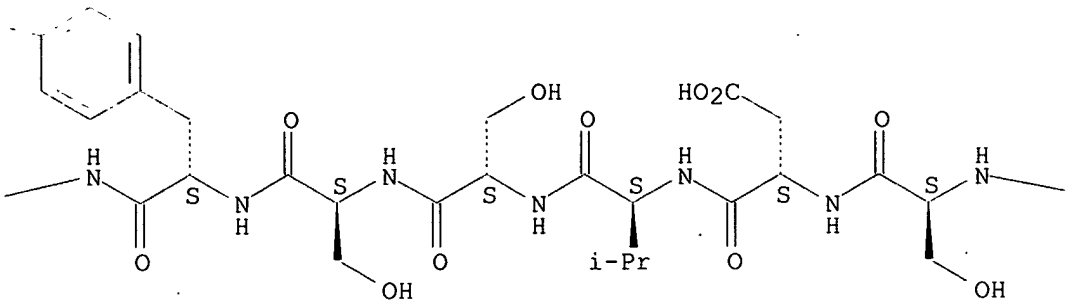
PAGE 1-A



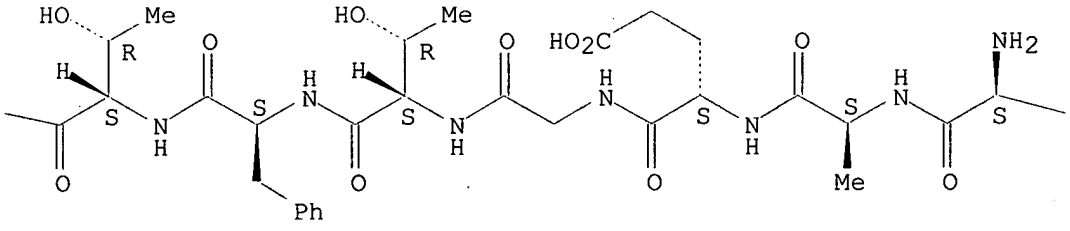
PAGE 1-B



PAGE 1-C



PAGE 1-D



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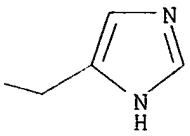


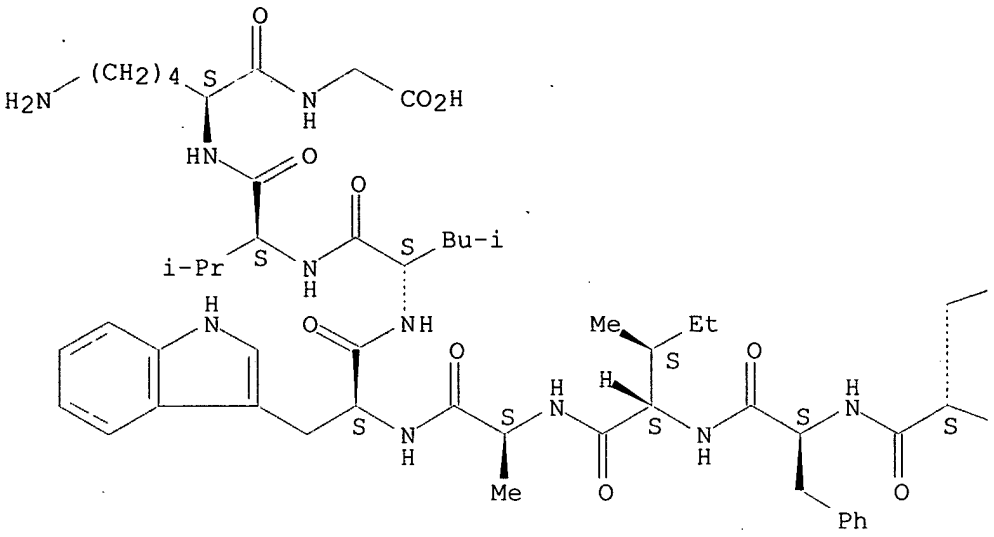
L59 ANSWER 8 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1989:614921 HCAPLUS
DN 111:214921
ED Entered STN: 09 Dec 1989
TI Synthesis of GLP-1 related peptides and production of GLP-1 specific antisera
AU Suzuki, Matsuaki; Ishikawa, Junji; Inoue, Takashi; Zhang, Tao; Mochizuki, Tohru; Kuwahara, Atsukara; Yonezu, Emiko; Hoshino, Minoru; Yanaihara, Chizuko; Yanaihara, Noboru
CS Natl. Inst. Physiol. Sci., Okazaki, Japan
SO Peptide Chemistry (**1989**), Volume Date 1988, 26th, 73-8
CODEN: PECHDP; ISSN: 0388-3698
DT Journal
LA English
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 2, 15
AB A report from a symposium. Nine GLP-1 (GLP = **glucagon**-like peptide) related peptides, e.g. GLP-1(1-37) and GLP-1(9-22), were prepared The production of GLP-1 specific antisera is described.
ST **glucagon** like peptide prepn symposium; immunochem
glucagon like peptide symposium
IT Antiserums
(of **glucagon**-like peptide-1 related peptides)
IT **89750-14-1**, **Glucagon**-related peptide I
RL: RCT (Reactant); RACT (Reactant or reagent)
(peptides related to, preparation and immunochem. of)
IT 87805-34-3P, **Glucagon**-related peptide I (ox) 106612-94-6P
121181-17-7P 123475-27-4P **123475-28-5P** 123475-29-6P
123475-30-9P 123475-31-0P 123512-62-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and immunochem. of)
IT **89750-14-1**, **Glucagon**-related peptide I
RL: RCT (Reactant); RACT (Reactant or reagent)
(peptides related to, preparation and immunochem. of)
RN 89750-14-1 HCAPLUS
CN Glucagon-like peptide I (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **123475-28-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and immunochem. of)

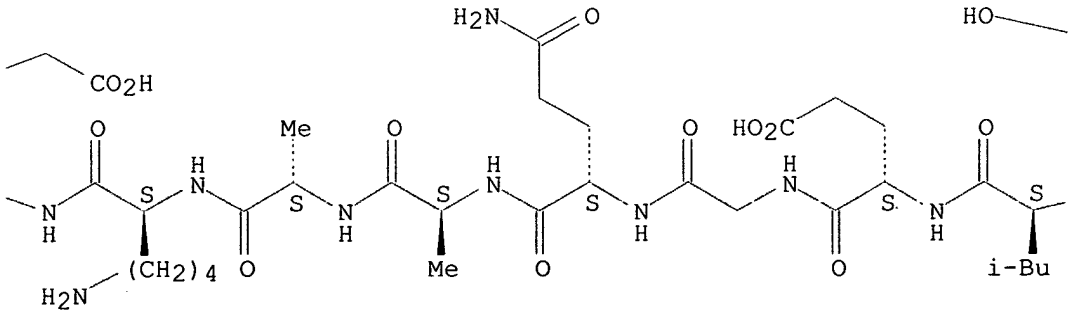
RN 123475-28-5 HCAPLUS
CN Glycine, L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-lysyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



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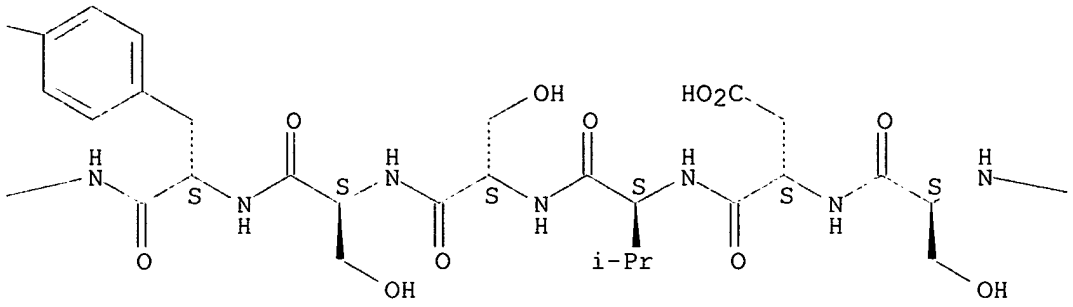
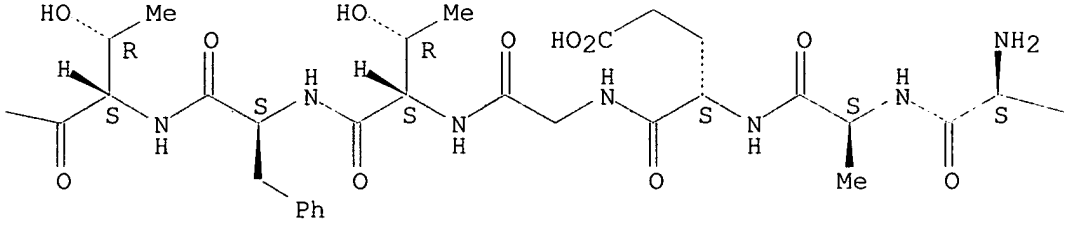
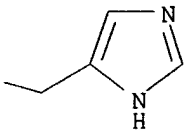


PAGE 1-D



PAGE 1-E



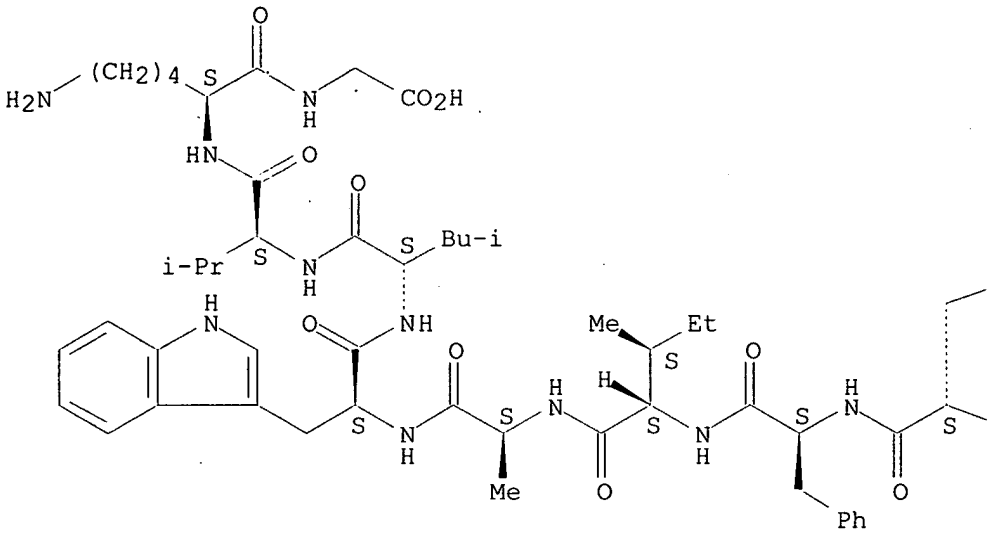
L59 ANSWER 9 OF 9 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1989:587711 HCAPLUS
DN 111:187711
ED Entered STN: 25 Nov 1989
TI **Glucagon**-like peptide-1: synthetic approach
AU Yanaihara, Chizuko; Suzuki, Mutsuaki; Ishikawa, Junji; Kurokawa, Nobuo; Yanaihara, Noboru
CS Med. Sch., Osaka Univ., Osaka, 553, Japan
SO Biomedical Research (**1988**), 9(Suppl. 3), 225-8
CODEN: BRESD5; ISSN: 0388-6107
DT Journal
LA English
CC 2-2 (Mammalian Hormones)
Section cross-reference(s): 34
AB **Glucagon**-like peptide-1 (GLP-1)-related peptides shortened in amino and (or) carboxyl-terminal portions of GLP-1(1-37) were synthesized and their insulinotropic potencies were assessed by the stimulating effect on 13.9 mM glucose-induced insulin release from isolated perfused rat pancreas. The synthetic peptides include: GLP-1(1-37), (1-36), (1-35), (7-37), (7-36), (7-35), (7-22), and (9-22). At 10-8M concentration, synthetic GLP-1(7-35) was the most potent of the 8 peptides examined and exhibited an insulin release-enhancing effect >3-fold stronger than that of 10-8M **glucagon**. Thus, GLP-1(7-35) can not be excluded from the candidate forms for endogenous GLP-1 related peptide(s).
ST **glucagon** like peptide fragment insulin; structure activity **glucagon** like peptide
IT Peptides, preparation
RL: PREP (Preparation)
(**glucagon**-like)
IT Molecular structure-biological activity relationship
(insulin-releasing, of **glucagon**-like peptide-1 and fragments)
IT 50-99-7, D-Glucose, biological studies
RL: BIOL (Biological study)
(insulin secretion stimulation by, **glucagon**-like peptide-1 and fragments effect on)
IT 87805-34-3P, **Glucagon**-related peptide I (ox)
89750-14-1DP, **Glucagon**-related peptide I, fragments
106612-94-6P 121181-17-7P 123475-27-4P **123475-28-5P**
123475-30-9P 123475-31-0P 123512-62-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and insulin release enhancing activity of, mol. structure in

relation to)
IT 9004-10-8, Insulin, biological studies
RL: BIOL (Biological study)
(secretion of, **glucagon**-like peptide-1 and fragments effect on)
IT **89750-14-1DP, Glucagon**-related peptide I, fragments
123475-28-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and insulin release enhancing activity of, mol. structure in relation to)
RN 89750-14-1 HCAPLUS
CN Glucagon-like peptide I (9CI) (CA INDEX NAME)

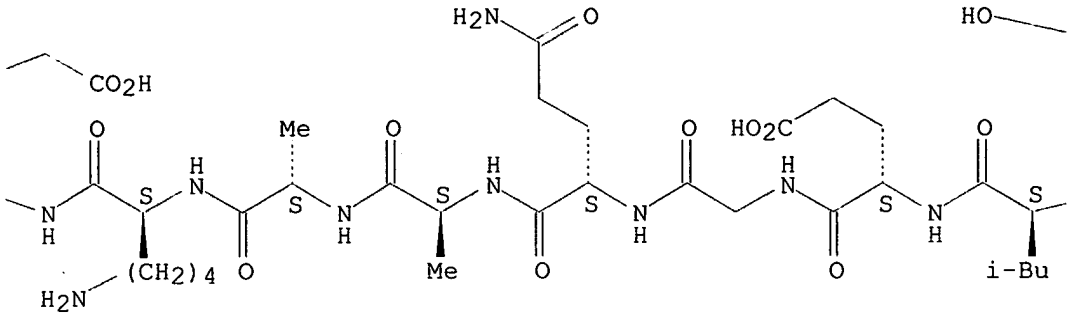
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 123475-28-5 HCAPLUS
CN Glycine, L-histidyl-L-alanyl-L-α-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-α-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-α-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-α-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-lysyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

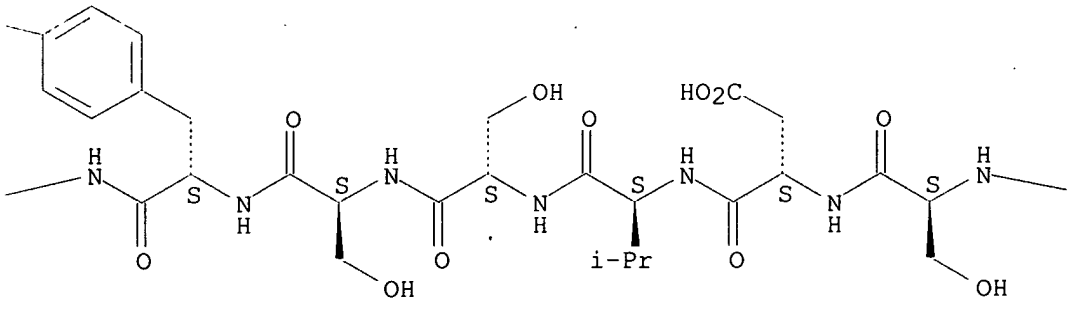
PAGE 1-A



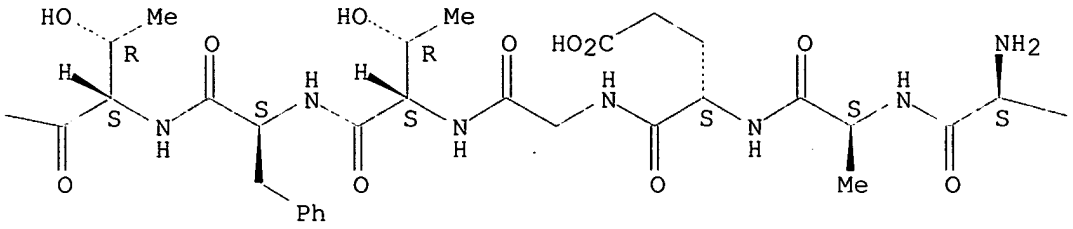
PAGE 1-B



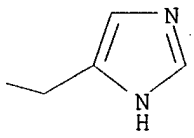
PAGE 1-C



PAGE 1-D



PAGE 1-E



=>

```
! FINDPATTERNS on pir:* allowing 0 mismatches

!        1 H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG                                  Ja


               GCHU  ck: 9748  len: 180   ! glucagon precursor [validated] - human

1                    H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                         H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
           98: DEFER        HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG        RRDFP


               GCGP  ck: 629   len: 180   ! glucagon precursor - guinea pig

1                    H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                         H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
           98: DEFER        HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG        RRDFP


             GCRTDU  ck: 736   len: 180   ! glucagon precursor - degu

1                    H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                         H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
           98: DEFER        HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG        RRDFP


               GCRT  ck: 9106  len: 180   ! glucagon precursor - rat

1                    H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                         H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
           98: DEFER        HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG        RRDFP


               GCHY  ck: 206   len: 180   ! glucagon precursor - golden hamster

1                    H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                         H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
           98: DEFER        HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG        RRDFP


               GCBO  ck: 2258  len: 180   ! glucagon precursor - bovine

1                    H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                         H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
           98: DEFER        HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG        RRDFP


               GCPG  ck: 106   len: 158   ! glucagon precursor - pig (fragment)

1                    H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                         H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
           78: XXXXX        HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG        XXDFP


              A57294  ck: 8386  len: 180   ! glucagon precursor - mouse

1                    H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                         H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
           98: DEFER        HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG        RRDFP


 Databases searched:
       NBRF, Release 76.1, Released on 12May2003, Formatted on 10Jun2003

    Total finds:              8
   Total length:     96,168,682
Total sequences:        283,308
       CPU time:       02:23.50
```

```
!!SEQUENCE_LIST 1.0
! FINDPATTERNS on pir:* allowing 0 mismatches

!        1 H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG                                  Ja

PIR1:GCHU              ck: 9748  len: 180    finds: 1    ! glucagon precursor [validated]
PIR1:GCGP              ck: 629   len: 180    finds: 1    ! glucagon precursor - guinea pi
PIR1:GCRTDU            ck: 736   len: 180    finds: 1    ! glucagon precursor - degu
PIR1:GCRT              ck: 9106  len: 180    finds: 1    ! glucagon precursor - rat
PIR1:GCHY              ck: 206   len: 180    finds: 1    ! glucagon precursor - golden ha
PIR1:GCBO              ck: 2258  len: 180    finds: 1    ! glucagon precursor - bovine
PIR1:GCPG              ck: 106   len: 158    finds: 1    ! glucagon precursor - pig (frag
PIR2:A57294            ck: 8386  len: 180    finds: 1    ! glucagon precursor - mouse

\\End of list

 Databases searched:
       NBRF, Release 76.1, Released on 12May2003, Formatted on 10Jun2003

     Total finds:              8
    Total length:     96,168,682
 Total sequences:        283,308
        CPU time:       03:06.52
```

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!!AA_SEQUENCE 1.0
P1;GCHU - glucagon precursor [validated] - human
N;Contains: glicentin; glicentin-related polypeptide (GRPP); glucagon;
 glucagon-like peptide 1 (GLP1); glucagon-like peptide 2 (GLP2); major
 proglucagon fragment; oxyntomodulin; truncated glucagon-like peptide 1 (tGLP1)
C;Species: Homo sapiens (man)
C;Date: 24-Apr-1984 #sequence_revision 31-Mar-1993 #text_change 08-Dec-2000
C;Accession: A24377; A44197; A30875; A32614; A01541; S23309
R;White, J.W.; Saunders, G.F.
Nucleic Acids Res. 14, 4719-4730, 1986
A;Title: Structure of the human glucagon gene.
A;Reference number: A24377; MUID:86259053; PMID:3725587
A;Accession: A24377
A;Molecule type: DNA
A;Residues: 1-180 <WHI>
A;Cross-references: GB:X03991
R;Bell, G.I.; Sanchez-Pescador, R.; Laybourn, P.J.; Najarian, R.C.
Nature 304, 368-371, 1983
A;Title: Exon duplication and divergence in the human preproglucagon gene.
A;Reference number: A44197; MUID:83271477; PMID:6877358
A;Accession: A44197
A;Molecule type: DNA
A;Residues: 1-179 <BEL>
A;Cross-references: GB:V01515; NID:g31777; PIDN:CAA24759.1; PID:g31778
R;Drucker, D.J.; Asa, S.
J. Biol. Chem. 263, 13475-13478, 1988
A;Title: Glucagon gene expression in vertebrate brain.
A;Reference number: A30875; MUID:88330860; PMID:2901414
A;Accession: A30875
A;Molecule type: mRNA
A;Residues: 1-180 <DRU>
A;Cross-references: GB:J04040; NID:g183269; PIDN:AAA52567.1; PID:g183270
R;Orskov, C.; Bersani, M.; Johnsen, A.H.; Hojrup, P.; Holst, J.J.
J. Biol. Chem. 264, 12826-12829, 1989
A;Title: Complete sequences of glucagon-like peptide-1 from human and pig small
 intestine.
A;Reference number: A92732; MUID:89327238; PMID:2753890
A;Accession: A32614
A;Molecule type: protein
A;Residues: 98-127 <ORS>
R;Thomsen, J.; Kristiansen, K.; Brunfeldt, K.; Sundby, F.
FEBS Lett. 21, 315-319, 1972
A;Title: The amino acid sequence of human glucagon.
A;Reference number: A91373
A;Accession: A01541
A;Molecule type: protein
A;Residues: 53-81 <THO>
R;Tsugita, A.; Takamoto, K.; Kamo, M.; Iwadate, H.
Eur. J. Biochem. 206, 691-696, 1992
A;Title: C-terminal sequencing of protein. A novel partial acid hydrolysis and
 analysis by mass spectrometry.
A;Reference number: S23188; MUID:92298996; PMID:1606956
A;Accession: S23309
A;Molecule type: protein
A;Residues: 53-81 <TSU>
C;Comment: In pancreatic alpha-cells, proglucagon is processed to
 glicentin-related polypeptide, glucagon, and major proglucagon fragment that is
 further processed to glucagon-like peptide 1. In intestinal L cells,
 proglucagon is processed to truncated glucagon-like peptide 1, glucagon-like
 peptide 2, and glicentin that is partially further processed to
 glicentin-related polypeptide and oxyntomodulin.
C;Genetics:
A;Gene: GDB:GCG
A;Cross-references: GDB:119265; OMIM:138030
A;Map position: 2q36-2q37
A;Introns: 31/2; 85/2; 131/2; 179/2
C;Superfamily: glucagon
C;Keywords: amidated carboxyl end; carbohydrate metabolism; duplication;
 hormone; intestine; pancreas
F;1-20/Domain: signal sequence #status predicted <SIG>
F;21-180/Product: proglucagon #status experimental <PGC>
F;21-89/Product: glicentin #status experimental <GLN>
F;21-50/Product: glicentin-related polypeptide #status predicted <GRPP>
F;53-89/Product: oxyntomodulin #status experimental <OXN>
F;53-81/Product: glucagon #status experimental <GCN>
F;92-178/Product: major proglucagon fragment #status experimental <MPGF>
F;92-127/Product: glucagon-like peptide 1 #status experimental <GL1>
F;98-127/Product: truncated glucagon-like peptide 1 #status experimental <TGL>
F;146-178/Product: glucagon-like peptide 2 #status predicted <GL2>
F;127/Modified site: amidated carboxyl end (Arg) (amide in mature form from
 following glycine) #status experimental

  GCHU  Length: 180  January 22, 2004 17:52  Type: P  Check: 9758  ..

       1  MKSIYFVAGL FVMLVQGSWQ RSLQDTEEKS RSFSASQADP LSDPDQMNED

      51  KRHSQGTFTS DYSKYLDSRR AQDFVQWLMN TKRNRNNIAK RHDEFERHAE

     101  GTFTSDVSSY LEGQAAKEFI AWLVKGRGRR DFPEEVAIVE ELGRRHADGS

     151  FSDEMNTILD NLAARDFINW LIQTKITDRK

!!AA_SEQUENCE 1.0
P1;GCGP - glucagon precursor - guinea pig
N;Alternate names: oxyntomodulin
N;Contains: glicentin-related peptide; glucagon; glucagon-37 (oxyntomodulin);
 glucagon-like peptide 1; glucagon-like peptide 2
C;Species: Cavia porcellus (guinea pig)
C;Date: 30-Sep-1987 #sequence_revision 31-Dec-1992 #text_change 16-Jun-2000
C;Accession: A24856; A23849; A60323
R;Seino, S.; Welsh, M.; Bell, G.I.; Chan, S.J.; Steiner, D.F.
FEBS Lett. 203, 25-30, 1986
A;Title: Mutations in the guinea pig preproglucagon gene are restricted to a
 specific portion of the prohormone sequence.
A;Reference number: A24856; MUID:86248118; PMID:3755107
A;Accession: A24856
A;Molecule type: mRNA
A;Residues: 1-180 <SEI>
A;Cross-references: DDBJ:D00014; GB:N00014; NID:g220288; PIDN:BAA00010.1;
 PID:g220289
R;Huang, C.G.; Eng, J.; Pan, Y.C.E.; Hulmes, J.D.; Yalow, R.S.
Diabetes 35, 508-512, 1986
A;Title: Guinea pig glucagon differs from other mammalian glucagons.
A;Reference number: A23849; MUID:86165412; PMID:3956884
A;Accession: A23849
A;Molecule type: protein
A;Residues: 53-81 <HUA>
R;Conlon, J.M.; Hansen, H.F.; Schwartz, T.W.
Regul. Pept. 11, 309-320, 1985
A;Title: Primary structure of glucagon and a partial sequence of oxyntomodulin
 (glucagon-37) from the guinea pig.
A;Reference number: A60323; MUID:86017849; PMID:4048553
A;Accession: A60323
A;Molecule type: protein
A;Residues: 53-81 <CON>
A;Note: glucagon-37 was not completely sequenced
C;Superfamily: glucagon
C;Keywords: amidated carboxyl end; carbohydrate metabolism; duplication;
 hormone; pancreas
F;1-20/Domain: signal sequence #status predicted <SIG>
F;21-180/Product: proglucagon #status predicted <PGC>
F;21-50/Region: glicentin-related peptide #status predicted
F;53-89/Product: glucagon-37 (oxyntomodulin) #status experimental <G37>
F;53-81/Product: glucagon #status experimental <GCN>
F;98-127/Product: glucagon-like peptide 1 #status predicted <GL1>
F;146-178/Product: glucagon-like peptide 2 #status predicted <GL2>
F;127/Modified site: amidated carboxyl end (Arg) (amide in mature form from
 following glycine) #status predicted

  GCGP  Length: 180  January 22, 2004 17:52  Type: P  Check: 629  ..

       1  MKSVYFVAGL FIMLAQGSWQ RSLQDTEEKP RSVSASQTDM LDDPDQMNED

      51  KRHSQGTFTS DYSKYLDSRR AQQFLKWLLN VKRNRNNIAK RHDEFERHAE

     101  GTFTSDVSSY LEGQAAKEFI AWLVKGRGRR DFPEEVAIVE ELGRRHADGS
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    151  FSDEMNTILD NLATRDFINW LIQTKITDRK

!!AA_SEQUENCE 1.0
P1;GCRTDU - glucagon precursor - degu
N;Contains: glicentin-related peptide; glucagon; glucagon-like peptide 1;
 glucagon-like peptide 2
C;Species: Octodon degus (degu)
C;Date: 31-Mar-1993 #sequence_revision 31-Mar-1993 #text_change 18-Jun-1999
C;Accession: C36118
R;Nishi, M.; Steiner, D.F.
Mol. Endocrinol. 4, 1192-1198, 1990
A;Title: Cloning of complementary DNAs encoding islet amyloid polypeptide,
 insulin, and glucagon precursors from a New World rodent, the degu, Octodon
 degus.
A;Reference number: A36118; MUID:91155952; PMID:2293024
A;Accession: C36118
A;Molecule type: mRNA
A;Residues: 1-180 <NIS>
A;Cross-references: GB:M57688; NID:g202467; PIDN:AAA40588.1; PID:g202468
C;Superfamily: glucagon
C;Keywords: amidated carboxyl end; carbohydrate metabolism; duplication;
 hormone; pancreas
F;1-20/Domain: signal sequence #status predicted <SIG>
F;21-180/Product: proglucagon #status predicted <PGC>
F;21-50/Region: glicentin-related peptide #status predicted
F;53-81/Product: glucagon #status predicted <GCN>
F;98-127/Product: glucagon-like peptide 1 #status predicted <GL1>
F;146-178/Product: glucagon-like peptide 2 #status predicted <GL2>
F;127/Modified site: amidated carboxyl end (Arg) (amide in mature form from
 following glycine) #status predicted

  GCRTDU  Length: 180  January 22, 2004 17:52  Type: P  Check: 736  ..

       1  MKSIYFVAGL FVMLVQGSWQ HPLQDTEEKP RSFSTSQTDL LDDPDQMNED

      51  KRHSQGTFTS DYSKFLDTRR AQDFLDWLKN TKRNRNEIAK RHDEFERHAE

     101  GTFTSDVSSY LEGQAAKEFI AWLVKGRGRR DFPEEVTIVE ELRRRHADGS

     151  FSDEMNTVLD HLATKDFINW LIQTKITDRK

!!AA_SEQUENCE 1.0
P1;GCRT - glucagon precursor - rat
N;Contains: glicentin-related peptide; glucagon; glucagon-like peptide 1;
 glucagon-like peptide 2
C;Species: Rattus norvegicus (Norway rat)
C;Date: 30-Sep-1987 #sequence_revision 30-Sep-1987 #text_change 26-Feb-1999
C;Accession: A22655; A25190; A44198
R;Heinrich, G.; Gros, P.; Habener, J.F.
J. Biol. Chem. 259, 14082-14087, 1984
A;Title: Glucagon gene sequence: four of six exons encode separate functional
 domains of rat pre-proglucagon.
A;Reference number: A22655; MUID:85054853; PMID:6094539
A;Accession: A22655
A;Molecule type: DNA
A;Residues: 1-180 <HEI>
A;Cross-references: EMBL:K02809
A;Note: the authors translated the codon TTG for residue 10 as Glu and ACC for
 residue 59 as Pro
R;Mojsov, S.; Heinrich, G.; Wilson, I.B.; Ravazzola, M.; Orci, L.; Habener, J.F.
J. Biol. Chem. 261, 11880-11889, 1986
A;Title: Preproglucagon gene expression in pancreas and intestine diversifies
 at the level of post-translational processing.
A;Reference number: A25190; MUID:86304324; PMID:3528148
A;Accession: A25190
A;Status: not compared with conceptual translation
A;Molecule type: mRNA
A;Residues: 1-180 <MOJ>
R;Heinrich, G.; Gros, P.; Lund, P.K.; Bentley, R.C.; Habener, J.F.
Endocrinology 115, 2176-2181, 1984
A;Title: Pre-proglucagon messenger ribonucleic acid: nucleotide and encoded
 amino acid sequences of the rat pancreatic complementary deoxyribonucleic acid.
A;Reference number: A44198; MUID:85051023; PMID:6548696
A;Accession: A44198
A;Status: preliminary
A;Molecule type: mRNA
A;Residues: 1-180 <HE2>
A;Cross-references: GB:K02809; GB:K02810; GB:K02811; GB:K02812
C;Genetics:
A;Introns: 31/2; 85/2; 131/2; 179/2
C;Superfamily: glucagon
C;Keywords: amidated carboxyl end; carbohydrate metabolism; duplication;
 hormone; pancreas
F;1-20/Domain: signal sequence #status predicted <SIG>
F;21-180/Product: proglucagon #status predicted <PGC>
F;21-50/Region: glicentin-related peptide #status predicted
F;53-81/Product: glucagon #status predicted <GCN>
F;98-127/Product: glucagon-like peptide 1 #status predicted <GL1>
F;146-180/Product: glucagon-like peptide 2 #status predicted <GL2>
F;127/Modified site: amidated carboxyl end (Arg) (amide in mature form from
 following glycine) #status predicted

  GCRT  Length: 180  January 22, 2004 17:52  Type: P  Check: 9106  ..

       1  MKTVYIVAGL FVMLVQGSWQ HAPQDTEENA RSFPASQTEP LEDPDQINED

      51  KRHSQGTFTS DYSKYLDSRR AQDFVQWLMN TKRNRNNIAK RHDEFERHAE

     101  GTFTSDVSSY LEGQAAKEFI AWLVKGRGRR DFPEEVAIAE ELGRRHADGS

     151  FSDEMNTILD NLATRDFINW LIQTKITDKK

!!AA_SEQUENCE 1.0
P1;GCHY - glucagon precursor - golden hamster
N;Contains: glicentin-related peptide; glucagon; glucagon-like peptide 1;
 glucagon-like peptide 2
C;Species: Mesocricetus auratus (golden hamster)
C;Date: 13-Jun-1983 #sequence_revision 13-Jun-1983 #text_change 20-Mar-1998
C;Accession: A01539
R;Bell, G.I.; Santerre, R.F.; Mullenbach, G.T.
Nature 302, 716-718, 1983
A;Title: Hamster preproglucagon contains the sequence of glucagon and two
 related peptides.
A;Reference number: A01539; MUID:83167563; PMID:6835407
A;Accession: A01539
A;Molecule type: mRNA
A;Residues: 1-180 <BEL>
A;Cross-references: EMBL:J00059
C;Superfamily: glucagon
C;Keywords: amidated carboxyl end; carbohydrate metabolism; duplication;
 hormone; pancreas
F;1-20/Domain: signal sequence #status predicted <SIG>
F;21-180/Product: proglucagon #status predicted <PGC>
F;21-50/Region: glicentin-related peptide #status predicted
F;53-81/Product: glucagon #status predicted <GCN>
F;98-127/Product: glucagon-like peptide 1 #status predicted <GL1>
F;146-180/Product: glucagon-like peptide 2 #status predicted <GL2>
F;127/Modified site: amidated carboxyl end (Arg) (amide in mature form from
 following glycine) #status predicted

  GCHY  Length: 180  January 22, 2004 17:52  Type: P  Check: 106  ..

       1  MKNIYIVAGF FCGAGQGSWQ HSLQDTEEKS RSFPASQTDP LEDPDQINED

      51  KRHSQGTFTS DYSKYLDSRR AQDFVQWLMN TKRNRNNIAK RHDEFERHAE

     101  GTFTSDVSSY LEGQAAKEFI AWLVKGRGRR DFPEEVTIVE ELGRRHADGS

     151  FSDEMNTILD SLATRDFINW LIQTKITDKK

!!AA_SEQUENCE 1.0
P1;GCBO - glucagon precursor - bovine
N;Contains: glicentin-related peptide; glucagon; glucagon-like peptide 1;
 glucagon-like peptide 2
C;Species: Bos primigenius taurus (cattle)
```

C;Date: 14-Nov-1983 #sequence_revision 14-Nov-1983 #text_change 20-Mar-1998
C;Accession: A93970; A92081; A01538
R;Lopez, L.C.; Frazier, M.L.; Su, C.J.; Kumar, A.; Saunders, G.F.
Proc. Natl. Acad. Sci. U.S.A. 80, 5485-5489, 1983
A;Title: Mammalian pancreatic preproglucagon contains three glucagon-related peptides.
A;Reference number: A93970; MUID:83299996; PMID:6577439
A;Accession: A93970
A;Molecule type: mRNA
A;Residues: 1-180 <LOP>
A;Cross-references: EMBL:K00107
R;Bromer, W.W.; Boucher, M.E.; Koffenberger Jr., J.E.
J. Biol. Chem. 246, 2822-2827, 1971
A;Title: Amino acid sequence of bovine glucagon.
A;Reference number: A92081; MUID:71166445; PMID:5102927
A;Accession: A92081
A;Molecule type: protein
A;Residues: 53-81 <BRO>
C;Superfamily: glucagon
C;Keywords: amidated carboxyl end; carbohydrate metabolism; duplication; hormone; pancreas
F;1-20/Domain: signal sequence #status predicted <SIG>
F;21-180/Product: proglucagon #status predicted <PGC>
F;21-50/Region: glicentin-related peptide #status predicted
F;53-81/Product: glucagon #status experimental <GCN>
F;98-127/Product: glucagon-like peptide 1 #status experimental <GL1>
F;146-178/Product: glucagon-like peptide 2 #status predicted <GL2>
F;127/Modified site: amidated carboxyl end (Arg) (amide in mature form from following glycine) #status predicted

GCBO Length: 180 January 22, 2004 17:52 Type: P Check: 2258 ..

1 MKSLYFVAGL FVMLVQGSWQ RSLQNTEEKS SSFPAPQTDP LGDPDQINED

51 KRHSQGTFTS DYSKYLDSRR AQDFVQWLMN TKRNKNNIAK RHDEFERHAE

101 GTFTSDVSSY LEGQAAKEFI AWLVKGRGRR DFPEEVNIVE ELRRRHADGS

151 FSDEMNYVLD SLATRDFINW LLQTKITDRK

!!AA_SEQUENCE 1.0
F1;GCPG - glucagon precursor - pig (fragment)
N;Alternate names: glicentin; oxyntomodulin
N;Contains: glicentin-related peptide; glucagon; glucagon-37 (oxyntomodulin); glucagon-69 (glicentin); glucagon-like peptide 1; glucagon-like peptide 2
C;Species: Sus scrofa domestica (domestic pig)
C;Date: 17-Dec-1982 #sequence_revision 31-Mar-1993 #text_change 20-Mar-1998
C;Accession: A01540; A60312; A91781; B32614; A28064
R;Thim, L.; Moody, A.J.
Regul. Pept. 2, 139-150, 1981
A;Title: The primary structure of porcine glicentin (proglucagon).
A;Reference number: A94233; MUID:81248172; PMID:6894800
A;Accession: A01540
A;Molecule type: protein
A;Residues: 1-69 <TH1>
R;Thim, L.; Moody, A.J.
Regul. Pept. Suppl. 2, S33, 1983
A;Title: Primary structure of a possible porcine proglucagon fragment.
A;Reference number: A60312
A;Accession: A60312
A;Molecule type: protein
A;Residues: 1-30 <TH2>
A;Note: this peptide is co-secreted with glucagon from the pancreas
R;Bromer, W.W.; Sinn, L.G.; Behrens, O.K.
J. Am. Chem. Soc. 79, 2807-2810, 1957
A;Title: The amino acid sequence of glucagon. V. Location of amide groups, acid degradation studies and summary of sequential evidence.
A;Reference number: A91781
A;Accession: A91781
A;Molecule type: protein
A;Residues: 33-61 <BRO>
R;Orskov, C.; Bersani, M.; Johnsen, A.H.; Hojrup, P.; Holst, J.J.
J. Biol. Chem. 264, 12826-12829, 1989
A;Title: Complete sequences of glucagon-like peptide-1 from human and pig small intestine.
A;Reference number: A92732; MUID:89327238; PMID:2753890
A;Accession: B32614
A;Molecule type: protein
A;Residues: 78-107 <ORS>
R;Buhl, T.; Thim, L.; Kofod, H.; Orskov, C.; Harling, H.; Holst, J.J.
J. Biol. Chem. 263, 8621-8624, 1988
A;Title: Naturally occurring products of proglucagon 111-160 in the porcine and human small intestine.
A;Reference number: A28064; MUID:88243712; PMID:3379036
A;Accession: A28064
A;Molecule type: protein
A;Residues: 111-158 <BUH>
C;Comment: X's represent missing amino acids, mostly basic, that are predicted to exist in proglucagon before cleavage after basic residues
C;Superfamily: glucagon
C;Keywords: amidated carboxyl end; carbohydrate metabolism; duplication; hormone; intestine; pancreas
F;1-69/Product: glucagon-69 #status experimental <G69>
F;1-30/Region: glicentin-related peptide #status experimental
F;33-69/Product: glucagon-37 #status predicted <G37>
F;33-61/Product: glucagon #status experimental <GCN>
F;78-107/Product: glucagon-like peptide 1 #status experimental <GL1>
F;126-158/Product: glucagon-like peptide 2 #status experimental <GL2>
F;107/Modified site: amidated carboxyl end (Arg) (amide in mature form from following glycine) #status experimental

GCPG Length: 158 January 22, 2004 17:52 Type: P Check: 106 ..

1 RSLQNTEEKS RSFPAPQTDP LDDPDQMTED KRHSQGTFTS DYSKYLDSRR

51 AQDFVQWLMN TKRNKNNIAX XXXXXXXHAE GTFTSDVSSY LEGQAAKEPI

101 AWLVKGRGXX DFPEEVTIVE ELGRRHADGS FSDEMNTVLD NLATRDFINW

151 LLHTKITD

!!AA_SEQUENCE 1.0
P1;A57294 - glucagon precursor - mouse
C;Species: Mus musculus (house mouse)
C;Date: 01-Dec-1995 #sequence_revision 01-Dec-1995 #text_change 16-Jul-1999
C;Accession: A57294; S49903
R;Rothenberg, M.E.; Eilertson, C.D.; Klein, K.; Zhou, Y.; Lindberg, I.; McDonald, J.K.; Mackin, R.B.; Noe, B.D.
J. Biol. Chem. 270, 10136-10146, 1995
A;Title: Processing of mouse proglucagon by recombinant prohormone convertase 1 and immunopurified prohormone convertase 2 in vitro.
A;Reference number: A57294; MUID:95247722; PMID:7730317
A;Accession: A57294
A;Status: preliminary
A;Molecule type: mRNA
A;Residues: 1-180 <ROT>
A;Cross-references: EMBL:Z46845; NID:g599880; PIDN:CAA86902.1; PID:g599881
C;Superfamily: glucagon
C;Keywords: carbohydrate metabolism; duplication; hormone; pancreas

A57294 Length: 180 January 22, 2004 17:52 Type: P Check: 8386 ..

1 MKTIYFVAGL LIMLVQGSWQ HALQDTEENP RSFPASQTEA HEDPDEMNED

51 KRHSQGTFTS DYSKYLDSRR AQDFVQWLMN TKRNRNNIAK RHDEFERHAE

101 GTFTSDVSSY LEGQAAKEFI AWLVKGRGRR DFPEEVAIAE ELGRRHADGS

151 FSDEMSTILD NLATRDFINW LIQTKITDKK

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! FINDPATTERNS on swp:* allowing 0 mismatches

!       1 H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG                                  Ja

         GLUC_BOVIN  ck: 2043  len: 180   ! P01272 bos taurus (bovine). glucagon precur

1                    H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                         H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
           98: DEFER        HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG        RRDFP

         GLUC_CAVPO  ck: 629   len: 180   ! P05110 cavia porcellus (guinea pig). glucag

1                    H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                         H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
           98: DEFER        HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG        RRDFP

         GLUC_HUMAN  ck: 9748  len: 180   ! P01275 homo sapiens (human). glucagon precu

1                    H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                         H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
           98: DEFER        HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG        RRDFP

         GLUC_MESAU  ck: 1008  len: 180   ! P01273 mesocricetus auratus (golden hamster

1                    H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                         H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
           98: DEFER        HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG        RRDFP

         GLUC_MOUSE  ck: 8386  len: 180   ! P55095 mus musculus (mouse). glucagon precu

1                    H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                         H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
           98: DEFER        HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG        RRDFP

         GLUC_OCTDE  ck: 736   len: 180   ! P22890 octodon degus (degu). glucagon precu

1                    H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                         H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
           98: DEFER        HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG        RRDFP

           GLUC_PIG  ck: 9476  len: 158   ! P01274 sus scrofa (pig). glucagon precursor

1                    H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                         H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
           78: XXXXX        HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG        RRDFP

           GLUC_RAT  ck: 9106  len: 180   ! P06883 rattus norvegicus (rat). glucagon pr

1                    H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                         H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
           98: DEFER        HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG        RRDFP

             Q8MJ25  ck: 9513  len: 176   ! Q8mj25 ovis aries (sheep). preproglucagon (

1                    H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                         H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
           98: DEFER        HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG        RRDFP

             Q95LG0  ck: 1777  len: 180   ! Q95lg0 canis familiaris (dog). preproglucag

1                    H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                         H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
           98: DEFER        HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG        RRDFP
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Databases searched:
SWISS-PROT, Release 41.1, Released on 6Jun2003, Formatted on 9Jun2003
SPTREMBL, Release 23.0, Released on 4Mar2003, Formatted on 7Mar2003

Total finds:	10
Total length:	305,079,309
Total sequences:	958,388
CPU time:	08:11.42

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!!SEQUENCE_LIST 1.0
! FINDPATTERNS on swp:* allowing 0 mismatches

!        1 H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG                    Ja

SW:GLUC_BOVIN          ck: 2043  len: 180    finds: 1    ! P01272 bos taurus (bovine). gl
SW:GLUC_CAVPO          ck: 629   len: 180    finds: 1    ! P05110 cavia porcellus (guinea
SW:GLUC_HUMAN          ck: 9748  len: 180    finds: 1    ! P01275 homo sapiens (human). g
SW:GLUC_MESAU          ck: 1008  len: 180    finds: 1    ! P01273 mesocricetus auratus (g
SW:GLUC_MOUSE          ck: 8386  len: 180    finds: 1    ! P55095 mus musculus (mouse). g
SW:GLUC_OCTDE          ck: 736   len: 180    finds: 1    ! P22890 octodon degus (degu). g
SW:GLUC_PIG            ck: 9476  len: 158    finds: 1    ! P01274 sus scrofa (pig). gluca
SW:GLUC_RAT            ck: 9106  len: 180    finds: 1    ! P06883 rattus norvegicus (rat)
SP_OM:Q8MJ25           ck: 9513  len: 176    finds: 1    ! Q8mj25 ovis aries (sheep). pre
SP_OM:Q95LG0           ck: 1777  len: 180    finds: 1    ! Q95lg0 canis familiaris (dog).

\\End of list

 Databases searched:
        SWISS-PROT, Release 41.1, Released on 6Jun2003, Formatted on 9Jun2003
        SPTREMBL, Release 23.0, Released on 4Mar2003, Formatted on 7Mar2003

     Total finds:              10
    Total length:     305,079,309
 Total sequences:         958,388
        CPU time:        10:32.02
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!!AA_SEQUENCE 1.0
ID   GLUC_BOVIN     STANDARD;      PRT;   180 AA.
AC   P01272;
DT   21-JUL-1986 (Rel. 01, Created)
DT   13-AUG-1987 (Rel. 05, Last sequence update)
DT   28-FEB-2003 (Rel. 41, Last annotation update)
DE   Glucagon precursor [Contains: Glicentin-related polypeptide (GRPP);
DE   Glucagon; Glucagon-like peptide 1 (GLP1); Glucagon-like peptide 2
DE   (GLP2)].
GN   GCG.
OS   Bos taurus (Bovine).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Cetartiodactyla; Ruminantia; Pecora; Bovoidea;
OC   Bovidae; Bovinae; Bos.
OX   NCBI_TaxID=9913;
RN   [1]
RP   SEQUENCE FROM N.A.
RX   MEDLINE=83299996; PubMed=6577439;
RA   Lopez L.C., Frazier M.L., Su C.-J., Kumar A., Saunders G.F.;
RT   "Mammalian pancreatic preproglucagon contains three glucagon-related
RT   peptides.";
RL   Proc. Natl. Acad. Sci. U.S.A. 80:5485-5489(1983).
RN   [2]
RP   SEQUENCE OF 53-81.
RX   MEDLINE=71166445; PubMed=5102927;
RA   Bromer W.W., Boucher M.E., Koffenberger J.E. Jr.;
RT   "Amino acid sequence of bovine glucagon.";
RL   J. Biol. Chem. 246:2822-2827(1971).
RN   [3]
RP   STRUCTURE BY NMR OF 53-81.
RX   MEDLINE=71166445; PubMed=6631957;
RA   Braun W., Wider G., Lee K.H., Wuthrich K.;
RT   "Conformation of glucagon in a lipid-water interphase by 1H nuclear
RT   magnetic resonance.";
RL   J. Mol. Biol. 169:921-948(1983).
CC   -!- FUNCTION: GLUCAGON PROMOTES HYDROLYSIS OF GLYCOGEN AND LIPIDS, AND
CC       RAISES THE BLOOD SUGAR LEVEL.
CC   -!- FUNCTION: GLP2 STIMULATES INTESTINAL GROWTH AND UPREGULATES VILLUS
CC       HEIGHT IN THE SMALL INTESTINE, CONCOMITANT WITH INCREASED CRYPT
CC       CELL PROLIFERATION AND DECREASED ENTEROCYTE APOPTOSIS.
CC   -!- INDUCTION: PRODUCED IN THE A CELLS OF THE ISLETS OF LANGERHANS
CC       IN RESPONSE TO A DROP IN BLOOD SUGAR CONCENTRATION.
CC   -!- SIMILARITY: BELONGS TO THE GLUCAGON FAMILY.
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CC   entities requires a license agreement (See http://www.isb-sib.ch/announce/
CC   or send an email to license@isb-sib.ch).
CC   ---------------------------------------------------------------------
DR   EMBL; K00107; AAA30538.1; -.
DR   PDB; 1KX6; 13-FEB-02.
DR   InterPro; IPR000532; Glucagon.
DR   Pfam; PF00123; hormone2; 3.
DR   PRINTS; PR00275; GLUCAGON.
DR   SMART; SM00070; GLUCA; 3.
DR   PROSITE; PS00260; GLUCAGON; 4.
KW   Glucagon family; Hormone; Cleavage on pair of basic residues; Signal;
KW   3D-structure.
FT   SIGNAL       1     20
FT   PEPTIDE     21     50       GLICENTIN-RELATED POLYPEPTIDE.
FT   PEPTIDE     53     81       GLUCAGON.
FT   PROPEP      84     89
FT   PEPTIDE     92    128       GLUCAGON-LIKE PEPTIDE 1.
FT   PROPEP     131    142
FT   PEPTIDE    146    178       GLUCAGON-LIKE PEPTIDE 2.
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GLUC_BOVIN  Length: 180  January 22, 2004 17:52  Type: P  Check: 2043  ..

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     101  GTFTSDVSSY LEGQAAKEFI AWLVKGRGRR DFPEEVNIVE ELRRRHADGS

     151  FSDEMNTVLD SLATRDFINW LLQTKITDRK

!!AA_SEQUENCE 1.0
ID   GLUC_CAVPO     STANDARD;      PRT;   180 AA.
AC   P05110;
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DT   13-AUG-1987 (Rel. 05, Last sequence update)
DT   28-FEB-2003 (Rel. 41, Last annotation update)
DE   Glucagon precursor [Contains: Glicentin-related polypeptide (GRPP);
DE   Glucagon; Glucagon-37 (Oxyntomodulin); Glucagon-like peptide 1 (GLP1);
DE   Glucagon-like peptide 2 (GLP2)].
GN   GCG.
OS   Cavia porcellus (Guinea pig).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Rodentia; Hystricognathi; Caviidae; Cavia.
OX   NCBI_TaxID=10141;
RN   [1]
RP   SEQUENCE FROM N.A.
RX   MEDLINE=86248118; PubMed=3755107;
RA   Seino S., Welsh M., Bell G.I., Chan S.J., Steiner D.F.;
RT   "Mutations in the guinea pig preproglucagon gene are restricted to a
RT   specific portion of the prohormone sequence.";
RL   FEBS Lett. 203:25-30(1986).
RN   [2]
RP   SEQUENCE OF 53-81.
RX   MEDLINE=86165412; PubMed=3956884;
RA   Huang C.G., Eng J., Pan Y.-C.E., Hulmes J.D., Yalow R.S.;
RT   "Guinea pig glucagon differs from other mammalian glucagons.";
RL   Diabetes 35:508-512(1986).
RN   [3]
RP   PARTIAL SEQUENCE OF 53-89.
RX   MEDLINE=86017849; PubMed=4048553;
RA   Conlon J.M., Hansen H.F., Schwartz T.W.;
RT   "Primary structure of glucagon and a partial sequence of
RT   oxyntomodulin (glucagon-37) from the guinea pig.";
RL   Regul. Pept. 11:309-320(1985).
CC   -!- FUNCTION: GLUCAGON PROMOTES HYDROLYSIS OF GLYCOGEN AND LIPIDS, AND
CC       RAISES THE BLOOD SUGAR LEVEL.
CC   -!- FUNCTION: GLP2 STIMULATES INTESTINAL GROWTH AND UPREGULATES VILLUS
CC       HEIGHT IN THE SMALL INTESTINE, CONCOMITANT WITH INCREASED CRYPT
CC       CELL PROLIFERATION AND DECREASED ENTEROCYTE APOPTOSIS.
CC   -!- INDUCTION: PRODUCED IN THE A CELLS OF THE ISLETS OF LANGERHANS
CC       IN RESPONSE TO A DROP IN BLOOD SUGAR CONCENTRATION.
CC   -!- SIMILARITY: BELONGS TO THE GLUCAGON FAMILY.
CC   ---------------------------------------------------------------------
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CC   entities requires a license agreement (See http://www.isb-sib.ch/announce/
CC   or send an email to license@isb-sib.ch).
CC   ---------------------------------------------------------------------
DR   EMBL; D00014; BAA00010.1; -.
DR   PIR; A24856; GCGP.
DR   HSSP; P01274; 1GCN.
DR   InterPro; IPR000532; Glucagon.
DR   Pfam; PF00123; hormone2; 3.
DR   PRINTS; PR00275; GLUCAGON.
DR   SMART; SM00070; GLUCA; 3.
DR   PROSITE; PS00260; GLUCAGON; 4.
KW   Glucagon family; Hormone; Cleavage on pair of basic residues; Signal.
FT   SIGNAL       1     20
FT   PEPTIDE     21     50       GLICENTIN-RELATED POLYPEPTIDE.
FT   PEPTIDE     53     81       GLUCAGON.
```

```
FT   PEPTIDE      53     89       GLUCAGON-37.
FT   PEPTIDE      92    128       GLUCAGON-LIKE PEPTIDE 1.
FT   PROPEP      131    143
FT   PEPTIDE     146    178       GLUCAGON-LIKE PEPTIDE 2.
SQ   SEQUENCE   180 AA;  20972 MW;  702FB181161D2776 CRC64;

GLUC_CAVPO  Length: 180  January 22, 2004 17:52  Type: P  Check: 629  ..

       1  MKSVYFVAGL FIMLAQGSWQ RSLQDTEEKP RSVSASQTDM LDDPDQMNED

      51  KRHSQGTFTS DYSKYLDSRR AQQFLKWLLN VKRNRNNIAK RHDEFERHAE

     101  GTFTSDVSSY LEGQAAKEFI AWLVKGRGRR DFPEEVAIVE ELGRRHADGS

     151  FSDEMNTILD NLATRDFINW LIQTKITDRK

!!AA_SEQUENCE 1.0
ID   GLUC_HUMAN     STANDARD;      PRT;   180 AA.
AC   P01275;
DT   21-JUL-1986 (Rel. 01, Created)
DT   13-AUG-1987 (Rel. 05, Last sequence update)
DT   15-SEP-2003 (Rel. 42, Last annotation update)
DE   Glucagon precursor [Contains: Glicentin-related polypeptide (GRPP);
DE   Glucagon; Glucagon-like peptide 1 (GLP1); Glucagon-like peptide 2
DE   (GLP2)].
GN   GCG.
OS   Homo sapiens (Human).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
OX   NCBI_TaxID=9606;
RN   [1]
RP   SEQUENCE FROM N.A.
RX   MEDLINE=88330860; PubMed=2901414;
RA   Drucker D.J., Asa S.;
RT   "Glucagon gene expression in vertebrate brain.";
RL   J. Biol. Chem. 263:13475-13478(1988).
RN   [2]
RP   SEQUENCE FROM N.A.
RX   MEDLINE=86259053; PubMed=3725587;
RA   White J.W., Saunders G.F.;
RT   "Structure of the human glucagon gene.";
RL   Nucleic Acids Res. 14:4719-4730(1986).
RN   [3]
RP   SEQUENCE FROM N.A.
RC   TISSUE=Liver;
RX   MEDLINE=83271477; PubMed=6877358;
RA   Bell G.I., Sanchez-Pescador R., Laybourn P.J., Najarian R.C.;
RT   "Exon duplication and divergence in the human preproglucagon gene.";
RL   Nature 304:368-371(1983).
RN   [4]
RP   SEQUENCE FROM N.A.
RC   TISSUE=Pancreas;
RX   MEDLINE=22388257; PubMed=12477932;
RA   Strausberg R.L., Feingold E.A., Grouse L.H., Derge J.G.,
RA   Klausner R.D., Collins F.S., Wagner L., Shenmen C.M., Schuler G.D.,
RA   Altschul S.F., Zeeberg B., Buetow K.H., Schaefer C.F., Bhat N.K.,
RA   Hopkins R.F., Jordan H., Moore T., Max S.I., Wang J., Hsieh F.,
RA   Diatchenko L., Marusina K., Farmer A.A., Rubin G.M., Hong L.,
RA   Stapleton M., Soares M.B., Bonaldo M.F., Casavant T.L., Scheetz T.E.,
RA   Brownstein M.J., Usdin T.B., Toshiyuki S., Carninci P., Prange C.,
RA   Raha S.S., Loquellano N.A., Peters G.J., Abramson R.D., Mullahy S.J.,
RA   Bosak S.A., McEwan P.J., McKernan K.J., Malek J.A., Gunaratne P.H.,
RA   Richards S., Worley K.C., Hale S., Garcia A.M., Gay L.J., Hulyk S.W.,
RA   Villalon D.K., Muzny D.M., Sodergren E.J., Lu X., Gibbs R.A.,
RA   Fahey J., Helton E., Ketteman M., Madan A., Rodrigues S., Sanchez A.,
RA   Whiting M., Madan A., Young A.C., Shevchenko Y., Bouffard G.G.,
RA   Blakesley R.W., Touchman J.W., Green E.D., Dickson M.C.,
RA   Rodriguez A.C., Grimwood J., Schmutz J., Myers R.M.,
RA   Butterfield Y.S.N., Krzywinski M.I., Skalska U., Smailus D.E.,
RA   Schnerch A., Schein J.E., Jones S.J.M., Marra M.A.;
RT   "Generation and initial analysis of more than 15,000 full-length
RT   human and mouse cDNA sequences.";
RL   Proc. Natl. Acad. Sci. U.S.A. 99:16899-16903(2002).
RN   [5]
RP   SEQUENCE OF 53-81.
RA   Thomsen J., Kristiansen K., Brunfeldt K., Sundby F.;
RT   "The amino acid sequence of human glucagon.";
RL   FEBS Lett. 21:315-319(1972).
RN   [6]
RP   SEQUENCE OF 98-127.
RX   MEDLINE=89327238; PubMed=2753890;
RA   Orskov C., Bersani M., Johnsen A.H., Hoejrup P., Holst J.J.;
RT   "Complete sequences of glucagon-like peptide-1 from human and pig
RT   small intestine.";
RL   J. Biol. Chem. 264:12826-12829(1989).
RN   [7]
RP   X-RAY CRYSTALLOGRAPHY (3.0 ANGSTROMS) OF 53-81.
RX   MEDLINE=98334683; PubMed=9667960;
RA   Sturm N.S., Lin Y., Burley S.K., Krstenansky J.L., Ahn J.M.,
RA   Azizeh B.Y., Trivedi D., Hruby V.J.;
RT   "Structure-function studies on positions 17, 18, and 21 replacement
RT   analogues of glucagon: the importance of charged residues and salt
RT   bridges in glucagon biological activity.";
RL   J. Med. Chem. 41:2693-2700(1998).
CC   -!- FUNCTION: GLUCAGON PROMOTES HYDROLYSIS OF GLYCOGEN AND LIPIDS, AND
CC       RAISES THE BLOOD SUGAR LEVEL.
CC   -!- FUNCTION: GLP2 STIMULATES INTESTINAL GROWTH AND UPREGULATES VILLUS
CC       HEIGHT IN THE SMALL INTESTINE, CONCOMITANT WITH INCREASED CRYPT
CC       CELL PROLIFERATION AND DECREASED ENTEROCYTE APOPTOSIS.
CC   -!- INDUCTION: PRODUCED IN THE A CELLS OF THE ISLETS OF LANGERHANS
CC       IN RESPONSE TO A DROP IN BLOOD SUGAR CONCENTRATION.
CC   -!- PHARMACEUTICAL: Available under the names Glucagon (Eli Lilly) and
CC       GlucaGen or Glucagon Novo Nordisk (Novo Nordisk). Used to treat
CC       severe hypoglycemia in insulin-dependent diabetics.
CC   -!- SIMILARITY: BELONGS TO THE GLUCAGON FAMILY.
CC   -!- DATABASE: NAME=Glucagon at Eli Lilly;
CC       NOTE=Clinical information on Eli Lilly glucagon products;
CC       WWW="http://www.lillyDiabetes.com/Products/PatientInfo.cfm".
CC   ---------------------------------------------------------------------
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CC   ---------------------------------------------------------------------
DR   EMBL; J04040; AAA52567.1; -.
DR   EMBL; X03991; CAA27627.1; -.
DR   EMBL; V01515; CAA24759.1; -.
DR   EMBL; BC005278; AAH05278.1; -.
DR   PIR; A24377; GCHU.
DR   PDB; 1BH0; 18-NOV-98.
DR   PDB; 1D0R; 23-OCT-02.
DR   Genew; HGNC:4191; GCG.
DR   MIM; 138030; -.
DR   MIM; 231530; -.
DR   GO; GO:0005625; C:soluble fraction; TAS.
DR   GO; GO:0008283; P:cell proliferation; TAS.
DR   GO; GO:0007631; P:feeding behavior; TAS.
DR   GO; GO:0007186; P:G-protein coupled receptor protein signalin. . .; TAS.
DR   GO; GO:0007165; P:signal transduction; TAS.
DR   InterPro; IPR000532; Glucagon.
DR   Pfam; PF00123; hormone2; 3.
DR   SMART; SM00070; GLUCA; 3.
DR   PROSITE; PS00260; GLUCAGON; 4.
KW   Glucagon family; Hormone; Cleavage on pair of basic residues; Signal;
KW   Pharmaceutical; 3D-structure; Polymorphism.
FT   SIGNAL       1     20
FT   PEPTIDE     21     50       GLICENTIN-RELATED POLYPEPTIDE.
FT   PEPTIDE     53     81       GLUCAGON.
FT   PROPEP      84     96
FT   PEPTIDE     98    127       GLUCAGON-LIKE PEPTIDE 1.
FT   PROPEP     131    143
FT   PEPTIDE    146    178       GLUCAGON-LIKE PEPTIDE 2.
FT   VARIANT    115    115       A -> V (IN dbSNP:5650).
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FT                                /FTId=VAR_014596.
FT   CONFLICT     82     82       K -> N (IN REF. 3).
FT   TURN         59     62
FT   HELIX        63     77
FT   TURN         78     79
SQ   SEQUENCE   180 AA;  20909 MW;  7A99EEC629B2862C CRC64;

GLUC_HUMAN  Length: 180  January 22, 2004 17:52  Type: P  Check: 9748  ..

       1  MKSIYFVAGL FVMLVQGSWQ RSLQDTEEKS RSFSASQADP LSDPDQMNED

      51  KRHSQGTFTS DYSKYLDSRR AQDFVQWLMN TKRNRNNIAK RHDEFERHAE

     101  GTFTSDVSSY LEGQAAKEFI AWLVKGRGRR DFPEEVAIVE ELGRRHADGS

     151  FSDEMNTILD NLAARDFINW LIQTKITDRK

!!AA_SEQUENCE 1.0
ID   GLUC_MESAU     STANDARD;      PRT;   180 AA.
AC   P01273;
DT   21-JUL-1986 (Rel. 01, Created)
DT   01-FEB-1996 (Rel. 33, Last sequence update)
DT   28-FEB-2003 (Rel. 41, Last annotation update)
DE   Glucagon precursor [Contains: Glicentin-related polypeptide (GRPP);
DE   Glucagon; Glucagon-like peptide 1 (GLP1); Glucagon-like peptide 2
DE   (GLP2)].
GN   GCG.
OS   Mesocricetus auratus (Golden hamster).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Cricetinae;
OC   Mesocricetus.
OX   NCBI_TaxID=10036;
RN   [1]
RP   SEQUENCE FROM N.A.
RX   MEDLINE=83167563; PubMed=6835407;
RA   Bell G.I., Santerre R.F., Mullenbach G.T.;
RT   "Hamster preproglucagon contains the sequence of glucagon and two
RT   related peptides.";
RL   Nature 302:716-718(1983).
RN   [2]
RP   REVISIONS TO 12-15.
RA   Bell G.I.;
RL   Submitted (XXX-1985) to the EMBL/GenBank/DDBJ databases.
CC   -!- FUNCTION: GLUCAGON PROMOTES HYDROLYSIS OF GLYCOGEN AND LIPIDS, AND
CC       RAISES THE BLOOD SUGAR LEVEL.
CC   -!- FUNCTION: GLP2 STIMULATES INTESTINAL GROWTH AND UPREGULATES VILLUS
CC       HEIGHT IN THE SMALL INTESTINE, CONCOMITANT WITH INCREASED CRYPT
CC       CELL PROLIFERATION AND DECREASED ENTEROCYTE APOPTOSIS.
CC   -!- INDUCTION: PRODUCED IN THE A CELLS OF THE ISLETS OF LANGERHANS
CC       IN RESPONSE TO A DROP IN BLOOD SUGAR CONCENTRATION.
CC   -!- SIMILARITY: BELONGS TO THE GLUCAGON FAMILY.
CC   ---------------------------------------------------------------------
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CC   use by non-profit institutions as long as its content is in no way
CC   modified and this statement is not removed. Usage by and for commercial
CC   entities requires a license agreement (See http://www.isb-sib.ch/announce/
CC   or send an email to license@isb-sib.ch).
CC   ---------------------------------------------------------------------
DR   EMBL; J00059; AAA37074.1; -.
DR   HSSP; P01274; 1GCN.
DR   InterPro; IPR000532; Glucagon.
DR   Pfam; PF00123; hormone2; 3.
DR   SMART; SM00070; GLUCA; 3.
DR   PROSITE; PS00260; GLUCAGON; 4.
KW   Glucagon family; Hormone; Cleavage on pair of basic residues; Signal.
FT   SIGNAL       1     20
FT   PEPTIDE     21     50       GLICENTIN-RELATED POLYPEPTIDE.
FT   PEPTIDE     53     81       GLUCAGON.
FT   PROPEP      84     89
FT   PEPTIDE     92    128       GLUCAGON-LIKE PEPTIDE 1.
FT   PROPEP     131    143
FT   PEPTIDE    146    178       GLUCAGON-LIKE PEPTIDE 2.
SQ   SEQUENCE   180 AA;  20954 MW;  02791B49D7AADD4B CRC64;

GLUC_MESAU  Length: 180  January 22, 2004 17:52  Type: P  Check: 1008  ..

       1  MKNIYIVAGF FVVLVQGSWQ HSLQDTEEKS RSFPASQTDP LEDPDQINED

      51  KRHSQGTFTS DYSKYLDSRR AQDFVQWLMN TKRNRNNIAK RHDEFERHAE

     101  GTFTSDVSSY LEGQAAKEFI AWLVKGRGRR DFPEEVTIVE ELGRRHADGS

     151  FSDEMNTILD SLATRDFINW LIQTKITDKK

!!AA_SEQUENCE 1.0
ID   GLUC_MOUSE     STANDARD;      PRT;   180 AA.
AC   P55095;
DT   01-OCT-1996 (Rel. 34, Created)
DT   01-OCT-1996 (Rel. 34, Last sequence update)
DT   28-FEB-2003 (Rel. 41, Last annotation update)
DE   Glucagon precursor [Contains: Glicentin-related polypeptide (GRPP);
DE   Glucagon; Glucagon-like peptide 1 (GLP1); Glucagon-like peptide 2
DE   (GLP2)].
GN   GCG.
OS   Mus musculus (Mouse).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
OX   NCBI_TaxID=10090;
RN   [1]
RP   SEQUENCE FROM N.A.
RC   TISSUE=Pancreatic islets;
RX   MEDLINE=95247722; PubMed=7730317;
RA   Rothenberg M.E., Eilertson C.D., Klein K., Zhou Y., Linberg I.,
RA   McDonald J.K., Mackin R.B., Noe B.D.;
RT   "Processing of mouse proglucagon by recombinant prohormone convertase
RT   1 and immunopurified prohormone convertase 2 in vitro.";
RL   J. Biol. Chem. 270:10136-10146(1995).
RN   [2]
RP   SEQUENCE FROM N.A.
RA   Shamsadin R., Knepel W.;
RT   "Mouse glucagon full length cDNA.";
RL   Submitted (JUN-2000) to the EMBL/GenBank/DDBJ databases.
CC   -!- FUNCTION: GLUCAGON PROMOTES HYDROLYSIS OF GLYCOGEN AND LIPIDS, AND
CC       RAISES THE BLOOD SUGAR LEVEL.
CC   -!- FUNCTION: GLP2 STIMULATES INTESTINAL GROWTH AND UPREGULATES VILLUS
CC       HEIGHT IN THE SMALL INTESTINE, CONCOMITANT WITH INCREASED CRYPT
CC       CELL PROLIFERATION AND DECREASED ENTEROCYTE APOPTOSIS.
CC   -!- INDUCTION: PRODUCED IN THE A CELLS OF THE ISLETS OF LANGERHANS
CC       IN RESPONSE TO A DROP IN BLOOD SUGAR CONCENTRATION.
CC   -!- SIMILARITY: BELONGS TO THE GLUCAGON FAMILY.
CC   ---------------------------------------------------------------------
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CC   entities requires a license agreement (See http://www.isb-sib.ch/announce/
CC   or send an email to license@isb-sib.ch).
CC   ---------------------------------------------------------------------
DR   EMBL; Z46845; CAA86902.1; -.
DR   EMBL; AF276754; AAK96898.1; -.
DR   PIR; A57294; A57294.
DR   HSSP; P01274; 1GCN.
DR   MGD; MGI:95674; Gcg.
DR   InterPro; IPR000532; Glucagon.
DR   Pfam; PF00123; hormone2; 3.
DR   PRINTS; PR00275; GLUCAGON.
DR   SMART; SM00070; GLUCA; 3.
DR   PROSITE; PS00260; GLUCAGON; 4.
KW   Glucagon family; Hormone; Cleavage on pair of basic residues; Signal.
FT   SIGNAL       1     20       BY SIMILARITY.
FT   PEPTIDE     21     50       GLICENTIN-RELATED POLYPEPTIDE.
FT   PEPTIDE     53     81       GLUCAGON.
FT   PROPEP      84     89
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FT   PEPTIDE      92    128       GLUCAGON-LIKE PEPTIDE 1.
FT   PROPEP      131    143
FT   PEPTIDE     146    178       GLUCAGON-LIKE PEPTIDE 2.
SQ   SEQUENCE   180 AA;  20906 MW;  595AA6DD9A589950 CRC64;

GLUC_MOUSE  Length: 180  January 22, 2004 17:52  Type: P  Check: 8386  ..

       1  MKTIYFVAGL LIMLVQGSWQ HALQDTEENP RSFPASQTEA HEDPDEMNED

      51  KRHSQGTFTS DYSKYLDSRR AQDFVQWLMN TKRNRNNIAK RHDEFERHAE

     101  GTFTSDVSSY LEGQAAKEFI AWLVKGRGRR DFPEEVAIAE ELGRRHADGS

     151  FSDEMSTILD NLATRDFINW LIQTKITDKK

!!AA_SEQUENCE 1.0
ID   GLUC_OCTDE     STANDARD;      PRT;   180 AA.
AC   P22890;
DT   01-AUG-1991 (Rel. 19, Created)
DT   01-AUG-1991 (Rel. 19, Last sequence update)
DT   28-FEB-2003 (Rel. 41, Last annotation update)
DE   Glucagon precursor [Contains: Glicentin-related polypeptide (GRPP);
DE   Glucagon; Glucagon-like peptide 1 (GLP1); Glucagon-like peptide 2
DE   (GLP2)].
GN   GCG.
OS   Octodon degus (Degu).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Rodentia; Hystricognathi; Octodontidae; Octodon.
OX   NCBI_TaxID=10160;
RN   [1]
RP   SEQUENCE FROM N.A.
RX   MEDLINE=91155952; PubMed=2293024;
RA   Nishi M., Steiner D.F.;
RT   "Cloning of complementary DNAs encoding islet amyloid polypeptide,
RT   insulin, and glucagon precursors from a New World rodent, the degu,
RT   Octodon degus.";
RL   Mol. Endocrinol. 4:1192-1198(1990).
CC   -!- FUNCTION: GLUCAGON PROMOTES HYDROLYSIS OF GLYCOGEN AND LIPIDS, AND
CC       RAISES THE BLOOD SUGAR LEVEL.
CC   -!- FUNCTION: GLP2 STIMULATES INTESTINAL GROWTH AND UPREGULATES VILLUS
CC       HEIGHT IN THE SMALL INTESTINE, CONCOMITANT WITH INCREASED CRYPT
CC       CELL PROLIFERATION AND DECREASED ENTEROCYTE APOPTOSIS.
CC   -!- INDUCTION: PRODUCED IN THE A CELLS OF THE ISLETS OF LANGERHANS
CC       IN RESPONSE TO A DROP IN BLOOD SUGAR CONCENTRATION.
CC   -!- SIMILARITY: BELONGS TO THE GLUCAGON FAMILY.
CC   ---------------------------------------------------------------------
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CC   use by non-profit institutions as long as its content is in no way
CC   modified and this statement is not removed. Usage by and for commercial
CC   entities requires a license agreement (See http://www.isb-sib.ch/announce/
CC   or send an email to license@isb-sib.ch).
CC   ---------------------------------------------------------------------
DR   EMBL; M57688; AAA40588.1; -.
DR   PIR; C36118; GCRTDU.
DR   HSSP; P01274; 1GCN.
DR   InterPro; IPR000532; Glucagon.
DR   Pfam; PF00123; hormone2; 3.
DR   PRINTS; PR00275; GLUCAGON.
DR   SMART; SM00070; GLUCA; 3.
DR   PROSITE; PS00260; GLUCAGON; 4.
KW   Glucagon family; Hormone; Cleavage on pair of basic residues; Signal;
KW   Amidation.
FT   SIGNAL        1     20
FT   PEPTIDE      21     50       GLICENTIN-RELATED POLYPEPTIDE.
FT   PEPTIDE      53     81       GLUCAGON.
FT   PROPEP       84     89
FT   PEPTIDE      92    127       GLUCAGON-LIKE PEPTIDE 1.
FT   PROPEP      131    142
FT   PEPTIDE     146    178       GLUCAGON-LIKE PEPTIDE 2.
FT   MOD_RES     127    127       AMIDATION (G-128 PROVIDE AMIDE GROUP).
SQ   SEQUENCE   180 AA;  21165 MW;  6E8836160A9A3051 CRC64;

GLUC_OCTDE  Length: 180  January 22, 2004 17:52  Type: P  Check: 736  ..

       1  MKSIYFVAGL FVMLVQGSWQ HPLQDTEEKP RSFSTSQTDL LDDPDQMNED

      51  KRHSQGTFTS DYSKFLDTRR AQDFLDWLKN TKRNRNEIAK RHDEFERHAE

     101  GTFTSDVSSY LEGQAAKEFI AWLVKGRGRR DFPEEVTIVE ELRRRHADGS

     151  FSDEMNTVLD HLATKDFINW LIQTKITDRK

!!AA_SEQUENCE 1.0
ID   GLUC_PIG       STANDARD;      PRT;   158 AA.
AC   P01274;
DT   21-JUL-1986 (Rel. 01, Created)
DT   01-NOV-1990 (Rel. 16, Last sequence update)
DT   28-FEB-2003 (Rel. 41, Last annotation update)
DE   Glucagon precursor [Contains: Glicentin; Glicentin-related polypeptide
DE   (GRPP); Glucagon; Glucagon-like peptide 1 (GLP1); Glucagon-like
DE   peptide 2 (GLP2)] (Fragment).
GN   GCG.
OS   Sus scrofa (Pig).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Cetartiodactyla; Suina; Suidae; Sus.
OX   NCBI_TaxID=9823;
RN   [1]
RP   SEQUENCE OF 1-69.
RX   MEDLINE=81248172; PubMed=6894800;
RA   Thim L., Moody A.J.;
RT   "The primary structure of porcine glicentin (proglucagon).";
RL   Regul. Pept. 2:139-150(1981).
RN   [2]
RP   SEQUENCE OF 1-69.
RX   MEDLINE=82221776; PubMed=7045833;
RA   Thim L., Moody A.J.;
RT   "The amino acid sequence of porcine glicentin.";
RL   Peptides 2 Suppl. 2:37-39(1981).
RN   [3]
RP   SEQUENCE OF 33-61.
RA   Bromer W.W., Sinn L.G., Behrens O.K.;
RT   "The amino acid sequence of glucagon. V. Location of amide groups,
RT   acid degradation studies and summary of sequential evidence.";
RL   J. Am. Chem. Soc. 79:2807-2810(1957).
RN   [4]
RP   SEQUENCE OF 78-107.
RX   MEDLINE=89327238; PubMed=2753890;
RA   Orskov C., Bersani M., Johnsen A.H., Hoejrup P., Holst J.J.;
RT   "Complete sequences of glucagon-like peptide-1 from human and pig
RT   small intestine.";
RL   J. Biol. Chem. 264:12826-12829(1989).
RN   [5]
RP   SEQUENCE OF 111-158.
RX   MEDLINE=88243712; PubMed=3379036;
RA   Buhl T., Thim L., Kofod H., Orskov C., Harling H., Holst J.J.;
RT   "Naturally occurring products of proglucagon 111-160 in the porcine
RT   and human small intestine.";
RL   J. Biol. Chem. 263:8621-8624(1988).
RN   [6]
RP   X-RAY CRYSTALLOGRAPHY (3.0 ANGSTROMS).
RX   MEDLINE=76051297; PubMed=171582;
RA   Sasaki K., Dockerill S., Adamiak D.A., Tickle I.J., Blundell T.L.;
RT   "X-ray analysis of glucagon and its relationship to receptor
RT   binding.";
RL   Nature 257:751-757(1975).
CC   -!- FUNCTION: GLUCAGON PROMOTES HYDROLYSIS OF GLYCOGEN AND LIPIDS, AND
CC       RAISES THE BLOOD SUGAR LEVEL.
CC   -!- FUNCTION: GLP2 STIMULATES INTESTINAL GROWTH AND UPREGULATES VILLUS
CC       HEIGHT IN THE SMALL INTESTINE, CONCOMITANT WITH INCREASED CRYPT
CC       CELL PROLIFERATION AND DECREASED ENTEROCYTE APOPTOSIS.
CC   -!- INDUCTION: PRODUCED IN THE A CELLS OF THE ISLETS OF LANGERHANS
CC       IN RESPONSE TO A DROP IN BLOOD SUGAR CONCENTRATION.
CC   -!- MISCELLANEOUS: X'S IN THE SEQUENCE WERE INCLUDED BY HOMOLOGY WITH
CC       HUMAN SEQUENCE.
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CC   -!- SIMILARITY: BELONGS TO THE GLUCAGON FAMILY.
DR   PDB; 1GCN; 30-SEP-83.
DR   InterPro; IPR000532; Glucagon.
DR   Pfam; PF00123; hormone2; 3.
DR   SMART; SM00070; GLUCA; 3.
DR   PROSITE; PS00260; GLUCAGON; 3.
KW   Glucagon family; Hormone; Cleavage on pair of basic residues;
KW   3D-structure.
FT   NON_TER       1      1
FT   PEPTIDE       1     69       GLICENTIN.
FT   PEPTIDE       1     30       GLICENTIN-RELATED POLYPEPTIDE.
FT   PEPTIDE      33     61       GLUCAGON.
FT   PEPTIDE      78    107       GLUCAGON-LIKE PEPTIDE 1.
FT   PEPTIDE     126    158       GLUCAGON-LIKE PEPTIDE 2.
FT   HELIX        39     42
FT   TURN         43     45
FT   HELIX        46     55
FT   TURN         56     57
SQ   SEQUENCE   158 AA;  18212 MW;  28C6FCF257F333B2 CRC64;

GLUC_PIG  Length: 158  January 22, 2004 17:52  Type: P  Check: 9476  ..

       1  RSLQNTEEKS RSFPAPQTDP LDDPDQMTED KRHSQGTFTS DYSKYLDSRR

      51  AQDFVQWLMN TKRNKNNIAX XXXXXXXHAE GTFTSDVSSY LEGQAAKEFI

     101  AWLVKGRGRR DFPEEVTIVE ELGRRHADGS FSDEMNTVLD NLATRDFINW

     151  LLHTKITD

!!AA_SEQUENCE 1.0
ID   GLUC_RAT       STANDARD;      PRT;   180 AA.
AC   P06883;
DT   01-JAN-1988 (Rel. 06, Created)
DT   01-JAN-1988 (Rel. 06, Last sequence update)
DT   28-FEB-2003 (Rel. 41, Last annotation update)
DE   Glucagon precursor [Contains: Glicentin-related polypeptide (GRPP);
DE   Glucagon; Glucagon-like peptide 1 (GLP1); Glucagon-like peptide 2
DE   (GLP2)].
GN   GCG.
OS   Rattus norvegicus (Rat).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Rattus.
OX   NCBI_TaxID=10116;
RN   [1]
RP   SEQUENCE FROM N.A.
RX   MEDLINE=85054853; PubMed=6094539;
RA   Heinrich G., Gros P., Habener J.F.;
RT   "Glucagon gene sequence. Four of six exons encode separate functional
RT   domains of rat pre-proglucagon.";
RL   J. Biol. Chem. 259:14082-14087(1984).
RN   [2]
RP   SEQUENCE FROM N.A.
RX   MEDLINE=85051023; PubMed=6548696;
RA   Heinrich G., Gros P., Lund P.K., Bentley R.C., Habener J.F.;
RT   "Pre-proglucagon messenger ribonucleic acid: nucleotide and encoded
RT   amino acid sequences of the rat pancreatic complementary
RT   deoxyribonucleic acid.";
RL   Endocrinology 115:2176-2181(1984).
RN   [3]
RP   SEQUENCE FROM N.A.
RX   MEDLINE=86304324; PubMed=3528148;
RA   Mojsov S., Heinrich G., Wilson I.B., Ravazzola M., Orci L.,
RA   Habener J.F.;
RT   "Preproglucagon gene expression in pancreas and intestine diversifies
RT   at the level of post-translational processing.";
RL   J. Biol. Chem. 261:11880-11889(1986).
CC   -!- FUNCTION: GLUCAGON PROMOTES HYDROLYSIS OF GLYCOGEN AND LIPIDS, AND
CC       RAISES THE BLOOD SUGAR LEVEL.
CC   -!- FUNCTION: GLP2 STIMULATES INTESTINAL GROWTH AND UPREGULATES VILLUS
CC       HEIGHT IN THE SMALL INTESTINE, CONCOMITANT WITH INCREASED CRYPT
CC       CELL PROLIFERATION AND DECREASED ENTEROCYTE APOPTOSIS.
CC   -!- INDUCTION: PRODUCED IN THE A CELLS OF THE ISLETS OF LANGERHANS
CC       IN RESPONSE TO A DROP IN BLOOD SUGAR CONCENTRATION.
CC   -!- SIMILARITY: BELONGS TO THE GLUCAGON FAMILY.
CC   ---------------------------------------------------------------------
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CC   or send an email to license@isb-sib.ch).
CC   ---------------------------------------------------------------------
DR   EMBL; K02813; AAA41235.1; -.
DR   EMBL; K02809; AAA41235.1; JOINED.
DR   EMBL; K02810; AAA41235.1; JOINED.
DR   EMBL; K02811; AAA41235.1; JOINED.
DR   EMBL; K02812; AAA41235.1; JOINED.
DR   PIR; A22655; GCRT.
DR   HSSP; P01274; 1GCN.
DR   InterPro; IPR000532; Glucagon.
DR   Pfam; PF00123; hormone2; 3.
DR   PRINTS; PR00275; GLUCAGON.
DR   SMART; SM00070; GLUCA; 3.
DR   PROSITE; PS00260; GLUCAGON; 4.
KW   Glucagon family; Hormone; Cleavage on pair of basic residues; Signal.
FT   SIGNAL        1     20
FT   PEPTIDE      21     50       GLICENTIN-RELATED POLYPEPTIDE.
FT   PEPTIDE      53     81       GLUCAGON.
FT   PROPEP       84     89
FT   PEPTIDE      92    128       GLUCAGON-LIKE PEPTIDE 1.
FT   PROPEP      131    143
FT   PEPTIDE     146    178       GLUCAGON-LIKE PEPTIDE 2.
SQ   SEQUENCE   180 AA;  20846 MW;  76931409D03C7978 CRC64;

GLUC_RAT  Length: 180  January 22, 2004 17:52  Type: P  Check: 9106  ..

       1  MKTVYIVAGL FVMLVQGSWQ HAPQDTEENA RSFPASQTEP LEDPDQINED

      51  KRHSQGTFTS DYSKYLDSRR AQDFVQWLMN TKRNRNNIAK RHDEFERHAE

     101  GTFTSDVSSY LEGQAAKEFI AWLVKGRGRR DFPEEVAIAE ELGRRADGS

     151  FSDEMNTILD NLATRDFINW LIQTKITDKK

!!AA_SEQUENCE 1.0
ID   Q8MJ25       PRELIMINARY;      PRT;   176 AA.
AC   Q8MJ25;
DT   01-OCT-2002 (TrEMBLrel. 22, Created)
DT   01-OCT-2002 (TrEMBLrel. 22, Last sequence update)
DT   01-MAR-2003 (TrEMBLrel. 23, Last annotation update)
DE   Preproglucagon (Fragment).
OS   Ovis aries (Sheep).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Cetartiodactyla; Ruminantia; Pecora; Bovoidea;
OC   Bovidae; Caprinae; Ovis.
OX   NCBI_TaxID=9940;
RN   [1]
RP   SEQUENCE FROM N.A.
RC   TISSUE=Pancreas;
RA   Limesand S.W., Hay W.W. Jr.;
RT   "Characterization of the endocrine pancreas in an ovine placental
RT   insufficiency IUGR fetus.";
RL   Submitted (JUL-2002) to the EMBL/GenBank/DDBJ databases.
DR   EMBL; AF529185; AAM94409.1; -.
DR   InterPro; IPR000532; Glucagon.
DR   Pfam; PF00123; hormone2; 3.
DR   PRINTS; PR00275; GLUCAGON.
DR   SMART; SM00070; GLUCA; 3.
DR   PROSITE; PS00260; GLUCAGON; 2.
FT   NON_TER     176    176
SQ   SEQUENCE   176 AA;  20335 MW;  13174039BD6CE2B3 CRC64;

 Q8MJ25  Length: 176  January 22, 2004 17:52  Type: P  Check: 9513  ..
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      1  MKSLYFVAGL LVMLAQGSWQ HSLQNTEEKS SSFPAPQTDP LGDPDQISED

     51  KRHSQGTFTS DYSKYLDSRR AQDFVQWLMN TKRNKNNIAK RHDEFERHAE

    101  GTFTSDVSSY LEGQAAKEFI AWLVKGRGRR DFPEEVNIVE ELRRRHADGS

    151  FSDEMNTVLD SLATRDFINW LLQTKI
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!!AA_SEQUENCE 1.0
ID   Q95LG0      PRELIMINARY;      PRT;   180 AA.
AC   Q95LG0;
DT   01-DEC-2001 (TrEMBLrel. 19, Created)
DT   01-DEC-2001 (TrEMBLrel. 19, Last sequence update)
DT   01-MAR-2003 (TrEMBLrel. 23, Last annotation update)
DE   Preproglucagon.
OS   Canis familiaris (Dog).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Carnivora; Fissipedia; Canidae; Canis.
OX   NCBI_TaxID=9615;
RN   [1]
RP   SEQUENCE FROM N.A.
RA   Irwin D.M.;
RT   "cDNA cloning of proglucagon from the stomach and pancreas of the
RT   dog.";
RL   Submitted (SEP-2000) to the EMBL/GenBank/DDBJ databases.
DR   EMBL; AF308439; AAL09425.1; -.
DR   InterPro; IPR000532; Glucagon.
DR   Pfam; PF00123; hormone2; 3.
DR   PRINTS; PR00275; GLUCAGON.
DR   SMART; SM00070; GLUCA; 3.
DR   PROSITE; PS00260; GLUCAGON; 2.
SQ   SEQUENCE   180 AA;  21114 MW;  80F66941AFC324FD CRC64;
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 Q95LG0  Length: 180  January 22, 2004 17:52  Type: P  Check: 1777  ..

      1  MKSIYFVAGL FVMLVQGSWQ RSLQDTEEKS RSFSAPQTEP LNDLDQMNED

     51  KRHSQGTFTS DYSKYLDSRR AQDFVQWLMN TKRNKNNIAK RHDEFERHAE

    101  GTFTSDVSSY LEGQAAKEFI AWLVKGRGRR DFPEEVAIVE EFRRRHADGS

    151  FSDEMNTVLD TLATRDFINW LLQTKITDRK
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! FINDPATTERNS on geneseqp:* allowing 0 mismatches
!       1 H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG                    Ja

        AAP71072  ck: 7361  len: 31    ! Aap71072 Insulinotropic peptide comprising

1               H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                    H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                    HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

        AAR07397  ck: 7361  len: 31    ! Aar07397 Glucagon-like peptide, GLP-1 (7-37

1               H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                    H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                    HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

        AAR13420  ck: 7361  len: 31    ! Aar13420 Glucagon-like peptide-1 (H)7-GLP-1

1               H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                    H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                    HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

        AAR13422  ck: 7361  len: 31    ! Aar13422 Glucagon-like peptide-1 (A)8-GLP-1

1               H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                    H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                    HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

        AAR13423  ck: 7361  len: 31    ! Aar13423 Glucagon-like peptide-1 (E)9-GLP-1

1               H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                    H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                    HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

        AAR42668  ck: 7361  len: 31    ! Aar42668 Glucagon-like peptide (GLP-1(7-37)

1               H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                    H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                    HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

        AAR45432  ck: 2897  len: 37    ! Aar45432 Glucagon-like peptide I derivative

1               H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                    H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 7: DEFER              HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

        AAR45434  ck: 7361  len: 31    ! Aar45434 Insulinotropin derivative. 3/2003

1               H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                    H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                    HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

        AAR63245  ck: 2897  len: 37    ! Aar63245 Glucagon-like peptide 1 (GLP-1) fc

1               H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                    H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 7: DEFER              HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

        AAR63246  ck: 7361  len: 31    ! Aar63246 Insulinotropin (GLP-1(7-37)) for u

1               H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                    H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                    HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

        AAR75885  ck: 7361  len: 31    ! Aar75885 Glucagon like peptide-1(7-36),

1               H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                    H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                    HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

        AAR69065  ck: 7361  len: 31    ! Aar69065 Glucagon like peptide 1 (GLP1)

1               H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                    H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                    HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

        AAR69076  ck: 2897  len: 37    ! Aar69076 Glucagon like peptide 1 (GLP1)

1               H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                    H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 7: DEFER              HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

        AAW03851  ck: 7361  len: 31    ! Aaw03851 Glucagon like peptide 1 (7-37)

1               H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                    H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                    HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

        AAW03907  ck: 7361  len: 31    ! Aaw03907 Glucagon like peptide 1 (7-37)

1               H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                    H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                    HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

        AAW03929  ck: 7361  len: 31    ! Aaw03929 Glucagon like peptide 1 (7-37)

1               H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                    H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                    HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

        AAW03899  ck: 7361  len: 31    ! Aaw03899 Glucagon like peptide 1 (7-37)

1               H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                    H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                    HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

        AAW03865  ck: 7361  len: 31    ! Aaw03865 Glucagon like peptide 1 (7-37)

1               H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                    H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                    HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

        AAW03866  ck: 7361  len: 31    ! Aaw03866 Glucagon like peptide 1 (7-37)

1               H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                    H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                    HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

        AAW03867  ck: 7361  len: 31    ! Aaw03867 Glucagon like peptide 1 (7-37)

1               H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                    H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                    HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

        AAW03853  ck: 7361  len: 31    ! Aaw03853 Glucagon like peptide 1 (7-3
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1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                     H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                    HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAW03854  ck: 7361  len: 31     ! Aaw03854 Glucagon like peptide 1 (7-37) ana

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                     H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                    HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAW03855  ck: 7361  len: 31     ! Aaw03855 Glucagon like peptide 1 (7-37) ana

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                     H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                    HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAW03873  ck: 7373  len: 31     ! Aaw03873 Glucagon like peptide 1 (7-37) ana

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                     H(G)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                    HGEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAW22079  ck: 8911  len: 180    ! Aaw22079 Rat preproglucagon. 2/1998

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                     H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
98: DEFER            HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG         ERDFP

AAW22080  ck: 9748  len: 180    ! Aaw22080 Human preproglucagon. 2/1998

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                     H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
98: DEFER            HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG         RRDFP

AAW22081  ck: 8864  len: 180    ! Aaw22081 Human preproglucagon mutant (R52A)

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                     H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
98: DEFER            HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG         RRDFP

AAW24389  ck: 7361  len: 31     ! Aaw24389 Glucagon-like peptide GLP-1(7-37)

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                     H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                    HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAW24390  ck: 7403  len: 31     ! Aaw24390 Glucagon-like peptide GLP-1(7-37)

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                     H(V)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                    HVEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAW16384  ck: 8962  len: 180    ! Aaw16384 Rat prepro-glucagon. 3/2003

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                     H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
98: DEFER            HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG         RRDFP

AAW63287  ck: 7361  len: 31     ! Aaw63287 Glucagon-like peptide-1 (7-37). 9/

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                     H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                    HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAW63289  ck: 7403  len: 31     ! Aaw63289 Val8-Glucagon-like peptide-1 (

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                     H(V)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                    HVEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAW63180  ck: 8034  len: 45     ! Aaw63180 GLP-1(1-45). 9/1998

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                     H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 7: DEFER            HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG         RRDFP

AAW63183  ck: 7361  len: 31     ! Aaw63183 GLP-1(7-37). 9/1998

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                     H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                    HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAW63184  ck: 9985  len: 32     ! Aaw63184 GLP-1(7-38). 9/1998

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                     H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                    HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG          R

AAW63185  ck: 2691  len: 33     ! Aaw63185 GLP-1(7-39). 9/1998

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                     H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                    HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG          RR

AAW63186  ck: 5003  len: 34     ! Aaw63186 GLP-1(7-40). 9/1998

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                     H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                    HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG          RRD

AAW63187  ck: 7453  len: 35     ! Aaw63187 GLP-1(7-41). 9/1998

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                     H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                    HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG          RRDF

AAW63190  ck: 2897  len: 37     ! Aaw63190 GLP-1(1-37). 9/1998

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                     H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 7: DEFER            HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAW63191  ck: 6013  len: 38     ! Aaw63191 GLP-1(1-38). 9/1998

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                     H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 7: DEFER            HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG          R

AAW63192  ck: 9211  len: 39     ! Aaw63192 GLP-1(1-39). 9/1998

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                     H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 7: DEFER            HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG          RR
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AAW63193 ck: 1931 len: 40 ! Aaw63193 GLP-1(1-40). 9/1998

1 H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
7: DEFER HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG RRD

AAW63194 ck: 4801 len: 41 ! Aaw63194 GLP-1(1-41). 9/1998

1 H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
7: DEFER HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG RRDF

AAW63195 ck: 7361 len: 31 ! Aaw63195 GLP-1(7-37). 9/1998

1 H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
1: HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAW50902 ck: 7361 len: 31 ! Aaw50902 Glucagon-like peptide-1 (7-37). 8/

1 H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
1: HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAY80306 ck: 7361 len: 31 ! Aay80306 Glucagon peptide-1 (7-37) analogue

1 H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
1: HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAY42936 ck: 7361 len: 31 ! Aay42936 Glucagon-like peptide GLP-1 (7-37)

1 H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
1: HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAY27375 ck: 7361 len: 31 ! Aay27375 Glucagon-like peptide 1 (GLP-1) fr

1 H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
1: HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAY39772 ck: 7361 len: 31 ! Aay39772 Glucagon like peptide-1 (7-37). 11

1 H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
1: HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAY39774 ck: 2897 len: 37 ! Aay39774 Glucagon like peptide-1 (1-37). 11

1 H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
7: DEFER HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAY39810 ck: 7361 len: 31 ! Aay39810 Glucagon-like peptide-1 (7-36). 11

1 H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
1: HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAY39812 ck: 9106 len: 180 ! Aay39812 Preproglucagon protein sequence. 1

1 H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
98: DEFER HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG RRDFP

AAY34199 ck: 7361 len: 31 ! Aay34199 GLP-1 mutant peptide, GLP-1(7-

1 H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
1: HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAY34200 ck: 9985 len: 32 ! Aay34200 GLP-1 mutant peptide, GLP-1(7-

1 H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
1: HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG R

AAY34201 ck: 2691 len: 33 ! Aay34201 GLP-1 mutant peptide, GLP-1(7-

1 H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
1: HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG RR

AAY34202 ck: 5003 len: 34 ! Aay34202 GLP-1 mutant peptide, GLP-1(7-

1 H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
1: HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG RRD

AAY34203 ck: 7453 len: 35 ! Aay34203 GLP-1 mutant peptide, GLP-1(7-

1 H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
1: HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG RRDF

AAY28960 ck: 5975 len: 187 ! Aay28960 Amino acid sequence of a fusic

1 H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
157: SRHKR HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAY28961 ck: 1204 len: 184 ! Aay28961 Amino acid sequence of a fusic

1 H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
154: SRHKR HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAY28962 ck: 1394 len: 184 ! Aay28962 Amino acid sequence of a fusic

1 H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
154: SRHPR HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAY28959 ck: 5814 len: 154 ! Aay28959 Amino acid sequence of a fusic

1 H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
124: SRHPR HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAY22165 ck: 7361 len: 31 ! Aay22165 GLP-1-like peptide. 9/1999

1 H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
1: HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

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AAY22167  ck: 7403  len: 31    ! Aay22167 GLP-1-like peptide. 9/1999

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                 H(V)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                 HVEGTFTSDVSSYLEGQAAKEFIAWLVKGRG


AAY18036  ck: 7361  len: 31    ! Aay18036 GLP-1(7-37)OH peptide. 8/1999

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                 H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                 HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG


AAB21328  ck: 7361  len: 31    ! Aab21328 GLP-1(7-37) peptide. 2/2001

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                 H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                 HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG


AAB21331  ck: 7403  len: 31    ! Aab21331 GLP-1 analogue Val8GLP-1(7-37). 2/

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                 H(V)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                 HVEGTFTSDVSSYLEGQAAKEFIAWLVKGRG


AAB21334  ck: 7373  len: 31    ! Aab21334 GLP-1 analogue Gly8-GLP-1(7-37). 2

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                 H(G)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                 HGEGTFTSDVSSYLEGQAAKEFIAWLVKGRG


AAB21339  ck: 7361  len: 31    ! Aab21339 GLP-1(7-37) peptide. 2/2001

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                 H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                 HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG


AAB21347  ck: 7403  len: 31    ! Aab21347 GLP-1 analogue #7. 2/2001

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                 H(V)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                 HVEGTFTSDVSSYLEGQAAKEFIAWLVKGRG


AAB21350  ck: 7373  len: 31    ! Aab21350 GLP-1 analogue #10. 2/2001

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                 H(G)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                 HGEGTFTSDVSSYLEGQAAKEFIAWLVKGRG


AAB21109  ck: 7361  len: 31    ! Aab21109 Human glucagon-like peptide-1 GLP-

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                 H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                 HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG


AAB23948  ck: 1498  len: 184   ! Aab23948 Plasmid pG117S4H ompRHPR protein e

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                 H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
154: SRHPR          HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG


AAB26773  ck: 8911  len: 180   ! Aab26773 Rat preproglucagon amino acid sequ

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                 H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 98: DEFER           HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG          ERDFP


AAB26774  ck: 9748  len: 180   ! Aab26774 Human preproglucagon amino ac:

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                 H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 98: DEFER           HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG          RRDFP


AAB26775  ck: 8864  len: 180   ! Aab26775 Mutant human preproglucagon a

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                 H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 98: DEFER           HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG          RRDFP


AAB26777  ck: 8646  len: 360   ! Aab26777 Human growth hormone and muta

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                 H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
278: DEFER          HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG          RRDFP


AAB11889  ck: 7403  len: 31    ! Aab11889 Shelf-stable glucagon-like pe

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                 H(V)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                 HVEGTFTSDVSSYLEGQAAKEFIAWLVKGRG


AAY96846  ck: 1278  len: 127   ! Aay96846 PCpB-QAR-V8-GLIP fusion prote:

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                 H(V)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 97: DSQAR           HVEGTFTSDVSSYLEGQAAKEFIAWLVKGRG


AAY96847  ck: 3743  len: 128   ! Aay96847 PCpB-LVPR-V8-GLIP fusion prot

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                 H(V)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 98: SLVPR           HVEGTFTSDVSSYLEGQAAKEFIAWLVKGRG


AAY53277  ck: 7361  len: 31    ! Aay53277 Glucagon-like peptide-1 analo

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                 H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                 HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG


AAY83149  ck: 7403  len: 31    ! Aay83149 Glucagon-like peptide-1. 7/20

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                 H(V)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                 HVEGTFTSDVSSYLEGQAAKEFIAWLVKGRG


AAY78950  ck: 7361  len: 31    ! Aay78950 Glucagon-like peptide-1 fragm

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                 H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                 HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG


AAY67372  ck: 7361  len: 31    ! Aay67372 Glucagon-like peptide-1 (7-37

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                 H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                 HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG
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AAY67374  ck: 2897  len: 37    ! Aay67374 Glucagon-like peptide-1 (1-37) ami

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                     H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 7: DEFER              HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG


ABG71251  ck: 2897  len: 37    ! Abg71251 Human glucagon-like peptide-1 (GLP

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                     H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 7: DEFER              HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG


ABG71253  ck: 7361  len: 31    ! Abg71253 Human glucagon-like peptide-1 (GLP

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                     H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                  HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG


AAE25338  ck: 7403  len: 31    ! Aae25338 Human glucagon-like peptide-1 rela

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                     H(V)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                  HVEGTFTSDVSSYLEGQAAKEFIAWLVKGRG


AAE25339  ck: 7361  len: 31    ! Aae25339 Human glucagon-like peptide-1 rela

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                     H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                  HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG


AAO22093  ck: 7361  len: 31    ! Aao22093 Glucagon-like peptide-1 (GLP-1), S

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                     H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                  HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG


ABB80094  ck: 2897  len: 37    ! Abb80094 Glucagon like peptide-1 (GLP-1) 1-

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                     H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 7: DEFER              HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG


ABB80096  ck: 7361  len: 31    ! Abb80096 Glucagon like peptide-1 (GLP-1) 7-

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                     H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                  HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG


ABB80861  ck: 7361  len: 31    ! Abb80861 Human glucagon-like peptide-1 (GLP

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                     H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                  HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG


ABB80862  ck: 7403  len: 31    ! Abb80862 Glucagon-like peptide-1 (GLP-1) Va

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                     H(V)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                  HVEGTFTSDVSSYLEGQAAKEFIAWLVKGRG


AAU85972  ck: 7361  len: 31    ! Aau85972 Modified human glucagon-like pepti

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                     H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                  HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG


AAE17659  ck: 7361  len: 31    ! Aae17659 Glucagon-like peptide-1 (GLP-1

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                     H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                  HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG


AAE17694  ck: 7403  len: 31    ! Aae17694 Glucagon-like peptide-1 (GLP-1

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                     H(V)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                  HVEGTFTSDVSSYLEGQAAKEFIAWLVKGRG


AAE14419  ck: 2897  len: 37    ! Aae14419 Mammalian glucagon-like peptid

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                     H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 7: DEFER              HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG


AAE14421  ck: 7361  len: 31    ! Aae14421 Mammalian glucagon-like peptid

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                     H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                  HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG


ABB07146  ck: 7361  len: 31    ! Abb07146 Glucagon-like peptide-1 (GLP-1

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                     H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                  HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG


AAM50391  ck: 2897  len: 37    ! Aam50391 Glucagon-like peptide 1. 2/200

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                     H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 7: DEFER              HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG


AAM50392  ck: 7361  len: 31    ! Aam50392 Glucagon-like peptide 1 (7-37)

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                     H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                  HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG


AAU07372  ck: 2897  len: 37    ! Aau07372 Mammalian glucagon-like peptid

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                     H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 7: DEFER              HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG


AAU07374  ck: 7361  len: 31    ! Aau07374 Mammalian glucagon-like peptid

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                     H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:                  HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG


AAE09251  ck: 7361  len: 31    ! Aae09251 Human glucagon-like peptide-1

1                H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
                     H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
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 1:              HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAE09266  ck: 7373  len: 31    ! Aae09266 Human DPP-IV protected glucagon-li
1           H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
             H(G)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:             HGEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAE09267  ck: 7403  len: 31    ! Aae09267 Human glucagon-like peptide-1 rela
1           H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
             H(V)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:             HVEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAE09278  ck: 7553  len: 31    ! Aae09278 Human glucagon-like peptide-1 rela
1           H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
             H(G)EGTFTSDVSSYL(Q)GQAAK(E)FIAWLVKGRG
 1:             HGEGTFTSDVSSYLQGQAAKEFIAWLVKGRG

AAG63268  ck: 7361  len: 31    ! Aag63268 Amino acid sequence of an insolubl
1           H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
             H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:             HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAG63272  ck: 7403  len: 31    ! Aag63272 Glucagon-like peptide 1 (GLP-1) an
1           H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
             H(V)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:             HVEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAG63280  ck: 7373  len: 31    ! Aag63280 An insoluble glucagon-like peptide
1           H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
             H(G)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:             HGEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAG63282  ck: 7403  len: 31    ! Aag63282 An insoluble glucagon-like peptide
1           H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
             H(V)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:             HVEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAG63302  ck: 7553  len: 31    ! Aag63302 An insoluble glucagon-like peptide
1           H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
             H(G)EGTFTSDVSSYL(Q)GQAAK(E)FIAWLVKGRG
 1:             HGEGTFTSDVSSYLQGQAAKEFIAWLVKGRG

AAB82335  ck: 7361  len: 31    ! Aab82335 Glucagon-like peptide 1 (7-37). 7/
1           H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
             H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:             HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAB91169  ck: 2897  len: 37    ! Aab91169 Pancreatic hormone glucagon peptid
1           H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
             H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 7: DEFER       HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAB30702  ck: 1397  len: 378   ! Aab30702 A Bacillus pectate lyase and h
1           H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
             H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
348: PASKR       HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAB30703  ck: 6043  len: 386   ! Aab30703 A Bacillus pectate lyase and h
1           H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
             H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
356: EPTKR       HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAB49694  ck: 7361  len: 31    ! Aab49694 Glucagon-like peptide 1 (GLP-1
1           H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
             H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:             HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAB49695  ck: 2897  len: 37    ! Aab49695 Glucagon-like peptide 1 (GLP-1
1           H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
             H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 7: DEFER       HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAB60246  ck: 2897  len: 37    ! Aab60246 Glucagon-like peptide-1, GLP-1
1           H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
             H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 7: DEFER       HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAB60248  ck: 7361  len: 31    ! Aab60248 Glucagon-like peptide-1, GLP-1
1           H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
             H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:             HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAB48790  ck: 2897  len: 37    ! Aab48790 Glucagon-like peptide 1 (GLP-1
1           H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
             H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 7: DEFER       HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAB48791  ck: 7361  len: 31    ! Aab48791 Glucagon-like peptide 1 derive
1           H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
             H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:             HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAB36413  ck: 2897  len: 37    ! Aab36413 Glucagon-like peptide-1 (1-37)
1           H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
             H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 7: DEFER       HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAB36415  ck: 7361  len: 31    ! Aab36415 Glucagon-like peptide-1 (7-37)
1           H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
             H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
 1:             HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAB36426  ck: 2897  len: 37    ! Aab36426 Glucagon-like peptide-1 (1-37)
1           H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
```

H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
7: DEFER HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAB36428 ck: 7361 len: 31 ! Aab36428 Glucagon-like peptide-1 (7-37) SEQ

1 H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
1: HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAB85919 ck: 2897 len: 37 ! Aab85919 Glucagon-like peptide-1 (GLP-1) fr

1 H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
7: DEFER HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAB85921 ck: 7361 len: 31 ! Aab85921 Glucagon-like peptide-1 (GLP-1) fr

1 H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
1: HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAE32655 ck: 3731 len: 52 ! Aae32655 GLP-1 (7-37)-human IgG1 mutant Fc

1 H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
1: HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG EPKSS

AAE32943 ck: 3731 len: 52 ! Aae32943 GLP-1 (7-37)-human IgG1 mutant Fc

1 H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
1: HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG EPKSS

AAE30127 ck: 7361 len: 31 ! Aae30127 Glucagon-like peptide-1 (GLP-1). 2

1 H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
1: HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAE30904 ck: 7361 len: 31 ! Aae30904 Human glucagon-like peptide 1, GLP

1 H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
1: HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAE30916 ck: 9940 len: 616 ! Aae30916 Val8-GLP-1-human serum albumin (HS

1 H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
H(V)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
1: HVEGTFTSDVSSYLEGQAAKEFIAWLVKGRG DAHKS

AAE30917 ck: 1796 len: 631 ! Aae30917 Val8-GLP-1-linker-human serum albu

1 H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
H(V)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
1: HVEGTFTSDVSSYLEGQAAKEFIAWLVKGRG GGGGS

AAE30921 ck: 1960 len: 264 ! Aae30921 Val8-GLP-1-Immunoglobulin G1 (IgG1

1 H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
H(V)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
1: HVEGTFTSDVSSYLEGQAAKEFIAWLVKGRG AEPKS

AAE30922 ck: 5244 len: 272 ! Aae30922 Val8-GLP-1-CBx-Immunoglobulin

1 H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
H(V)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
1: HVEGTFTSDVSSYLEGQAAKEFIAWLVKGRG SSGAP

AAE30953 ck: 7403 len: 31 ! Aae30953 Human GLP/exendin peptide anal

1 H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
H(V)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
1: HVEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAE30954 ck: 7361 len: 31 ! Aae30954 Human GLP/exendin peptide anal

1 H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
1: HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAE31010 ck: 7403 len: 31 ! Aae31010 Human GLP-1 analogue, Val8-GLP

1 H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
H(V)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
1: HVEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAE31011 ck: 7373 len: 31 ! Aae31011 Human GLP-1 analogue, Gly8-GLP

1 H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
H(G)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
1: HGEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAO19585 ck: 2897 len: 37 ! Aao19585 Mammalian GLP-1(1-37). 2/2003

1 H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
7: DEFER HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

AAO19587 ck: 7361 len: 31 ! Aao19587 Mammalian GLP-1(7-37). 2/2003

1 H(A,G,V)EGTFTSDVSSYL(E,Q)GQAAK(E,Q)FIAWLVKGRG
H(A)EGTFTSDVSSYL(E)GQAAK(E)FIAWLVKGRG
1: HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

Databases searched:
Geneseq-AA, Release 13.0, Released on 19Jun2003, Formatted on 15Jul2003

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Total length: 158,726,570
Total sequences: 1,107,863
CPU time: 05:46.96

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GENESEQP1990S:AAR13422 ck: 7361 len: 31 finds: 1 ! Aar13422 Glucagon-like pepti
GENESEQP1990S:AAR13423 ck: 7361 len: 31 finds: 1 ! Aar13423 Glucagon-like pepti
GENESEQP1990S:AAR42668 ck: 7361 len: 31 finds: 1 ! Aar42668 Glucagon-like pepti
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GENESEQP1990S:AAR45434 ck: 7361 len: 31 finds: 1 ! Aar45434 Insulinotropin deri
GENESEQP1990S:AAR63245 ck: 2897 len: 37 finds: 1 ! Aar63245 Glucagon-like pepti
GENESEQP1990S:AAR63246 ck: 7361 len: 31 finds: 1 ! Aar63246 Insulinotropin (GLP
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GENESEQP1990S:AAW63287 ck: 7361 len: 31 finds: 1 ! Aaw63287 Glucagon-like pepti
GENESEQP1990S:AAW63289 ck: 7403 len: 31 finds: 1 ! Aaw63289 Val8-Glucagon-like
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GENESEQP1990S:AAW63183 ck: 7361 len: 31 finds: 1 ! Aaw63183 GLP-1(7-37). 9/1998
GENESEQP1990S:AAW63184 ck: 9985 len: 32 finds: 1 ! Aaw63184 GLP-1(7-38). 9/
GENESEQP1990S:AAW63185 ck: 2691 len: 33 finds: 1 ! Aaw63185 GLP-1(7-39). 9/
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GENESEQP1990S:AAW63195 ck: 7361 len: 31 finds: 1 ! Aaw63195 GLP-1(7-37). 9/
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GENESEQP1990S:AAY39772 ck: 7361 len: 31 finds: 1 ! Aay39772 Glucagon like p
GENESEQP1990S:AAY39774 ck: 2897 len: 37 finds: 1 ! Aay39774 Glucagon like p
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GENESEQP1990S:AAY39812 ck: 9106 len: 180 finds: 1 ! Aay39812 Preproglucagon
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GENESEQP1990S:AAY34200 ck: 9985 len: 32 finds: 1 ! Aay34200 GLP-1 mutant pe
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GENESEQP1990S:AAY28959 ck: 5814 len: 154 finds: 1 ! Aay28959 Amino acid sequ
GENESEQP1990S:AAY22165 ck: 7361 len: 31 finds: 1 ! Aay22165 GLP-1-like pept
GENESEQP1990S:AAY22167 ck: 7403 len: 31 finds: 1 ! Aay22167 GLP-1-like pept
GENESEQP1990S:AAY18036 ck: 7361 len: 31 finds: 1 ! Aay18036 GLP-1(7-37)OH p
GENESEQP2000S:AAB21328 ck: 7361 len: 31 finds: 1 ! Aab21328 GLP-1(7-37) pep
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GENESEQP2000S:AAB26774 ck: 9748 len: 180 finds: 1 ! Aab26774 Human preproglucago
GENESEQP2000S:AAB26775 ck: 8864 len: 180 finds: 1 ! Aab26775 Mutant human prepro
GENESEQP2000S:AAB26777 ck: 8646 len: 360 finds: 1 ! Aab26777 Human growth hormon
GENESEQP2000S:AAB11889 ck: 7403 len: 31 finds: 1 ! Aab11889 Shelf-stable glucag
GENESEQP2000S:AAY96846 ck: 1278 len: 127 finds: 1 ! Aay96846 PCpB-QAR-V8-GLIP fu
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GENESEQP2002S:ABB80861 ck: 7361 len: 31 finds: 1 ! Abb80861 Human glucagon-like
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GENESEQP2002S:AAE17659 ck: 7361 len: 31 finds: 1 ! Aae17659 Glucagon-like pepti
GENESEQP2002S:AAE17694 ck: 7403 len: 31 finds: 1 ! Aae17694 Glucagon-like pepti
GENESEQP2002S:AAE14419 ck: 2897 len: 37 finds: 1 ! Aae14419 Mammalian glucagon-
GENESEQP2002S:AAE14421 ck: 7361 len: 31 finds: 1 ! Aae14421 Mammalian glucagon-
GENESEQP2002S:ABB07146 ck: 7361 len: 31 finds: 1 ! Abb07146 Glucagon-like pepti
GENESEQP2002S:AAM50391 ck: 2897 len: 37 finds: 1 ! Aam50391 Glucagon-like pepti
GENESEQP2002S:AAM50392 ck: 7361 len: 31 finds: 1 ! Aam50392 Glucagon-like pepti
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GENESEQP2001S:AAU07374 ck: 7361 len: 31 finds: 1 ! Aau07374 Mammalian glucagon-
GENESEQP2001S:AAE09251 ck: 7361 len: 31 finds: 1 ! Aae09251 Human glucagon-like
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GENESEQP2001S:AAE09267 ck: 7403 len: 31 finds: 1 ! Aae09267 Human glucagon-like
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GENESEQP2003S:AAE30917 ck: 1796 len: 631 finds: 1 ! Aae30917 Val8-GLP-1-link
GENESEQP2003S:AAE30921 ck: 1960 len: 264 finds: 1 ! Aae30921 Val8-GLP-1-Immu
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GENESEQP2003S:AAE30954 ck: 7361 len: 31 finds: 1 ! Aae30954 Human GLP/exend
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GENESEQP2003S:AAE31011 ck: 7373 len: 31 finds: 1 ! Aae31011 Human GLP-1 ana
GENESEQP2003S:AAO19585 ck: 2897 len: 37 finds: 1 ! Aao19585 Mammalian GLP-1
GENESEQP2003S:AAO19587 ck: 7361 len: 31 finds: 1 ! Aao19587 Mammalian GLP-1

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Databases searched:
Geneseq-AA, Release 13.0, Released on 19Jun2003, Formatted on 15Jul2003

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Total sequences:	1,107,863
CPU time:	08:09.51

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ID   AAP71072 standard; peptide; 31 AA.
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AC   AAP71072;
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DT   25-MAR-2003  (updated)
DT   03-OCT-2002  (updated)
DT   02-MAY-1991  (first entry)
XX
DE   Insulinotropic peptide comprising GLP-1 residues 7-37.
XX
KW   insulinotropic; glucagon like peptide; GLP-1; diabetes mellitus.
XX
OS   Homo sapiens.
XX
PN   WO8706941-A.
XX
PD   19-NOV-1987.
XX
PF   05-MAY-1987;   87WO-7001005.
XX
PR   05-MAY-1986;   86US-0859928.
XX
PA   (GEHO ) GEN HOSPITAL CORP.
XX
PI   Habener J;
XX
DR   WPI; 1987-334950/47.
XX
PT   New peptide derivs. - increase insulin prodn. from beta islet
PT   cells, comprise fragment of glucagon like peptide
XX
PS   Claim 1; Page 24; 35pp; English.
XX
CC   The mammalian hormone glucagon is produced as a precursor which is
CC   subsequently cleaved to yield three peptides, one of which is GLP-1.
CC   GLP-1 is itself processed in the pancreas and intestine from a 37
CC   amino acid long peptide to a 31 residue peptide (7-37) having the
CC   sequence given here. This insulinotropic hormone appears to act
CC   specifically on pancreatic Beta cells and as such is useful for
CC   enhancing insulin expression, eg for the treatment of diabetes
CC   mellitus.
CC   (Updated on 03-OCT-2002 to add missing OS field.)
CC   (Updated on 25-MAR-2003 to correct PA field.)
XX
SQ   Sequence   31 AA;

 AAP71072  Length: 31  January 22, 2004 18:02  Type: P  Check: 7361  ..

      1  HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID   AAR07397 standard; peptide; 31 AA.
XX
AC   AAR07397;
XX
DT   25-MAR-2003  (updated)
DT   29-JAN-1991  (first entry)
XX
DE   Glucagon-like peptide, GLP-1 (7-37).
XX
KW   Insulin; diabetes mellitus; insulinotropic: pancreatic beta cells.
XX
OS   Synthetic.
XX
PN   WO9011296-A.
XX
PD   04-OCT-1990.
XX
PF   20-MAR-1989;   89WO-US01121.
XX
PR   02-FEB-1989;   89US-0305458.
XX
PA   (GEHO ) GEN HOSPITAL CORP.
XX
PI   Habener JF;
XX
DR   WPI; 1990-320226/42.
XX
PT   New glucagon-like peptide (GLP-1) - having insulin
PT   formation-stimulating activity and useful in treating diabetes
PT   mellitus.
XX
PS   Claim 6; Page 39; 52pp; English.
XX
CC   The peptide has insulinotropic activity specifically for pancreatic
CC   beta cells. The peptide is derived from glucagon which, after
CC   synthesis is cleaved into three peptides: glucgon, glucagon-like
CC   peptide 1 (GLP-1) and GLP-2.  GLP-1 has 37 AAs in its unprocessed
CC   form and is unable to mediate the induction of insulin biosynthesis.
CC   It is, however, naturally converted to a 31 AA-long peptide having
CC   AAs 7-37 of GLP-1.  Preferred derivs. have an H2 gp at the
CC   N-terminal and an OH, OM, or NR'R'' gp at the C-terminal where M= a
CC   cation or lower alkyl gp., and R' and R''= H or a lower alkyl gp.
CC   Prepns. contg. the peptide or derivs. are useful in the study of
CC   the pathogenesis of maturity onset of diabetes mellitus and also in
CC   therapy.
CC   (Updated on 25-MAR-2003 to correct PR field.)
CC   (Updated on 25-MAR-2003 to correct PA field.)
XX
SQ   Sequence   31 AA;

 AAR07397  Length: 31  January 22, 2004 18:02  Type: P  Check: 7361  ..

      1  HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID   AAR13420 standard; Protein; 31 AA.
XX
AC   AAR13420;
XX
DT   29-OCT-1991  (first entry)
XX
DE   Glucagon-like peptide-1 (H)7-GLP-1(7-37).
XX
KW   Glucagon; insulin; diabetes; degradation; islet cells.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Modified-site   1
FT                   /label= D-H, N-acetyl-H, N-isopropyl-H
XX
PN   WO9111457-A.
XX
PD   08-AUG-1991.
XX
PF   24-JAN-1991;   91WO-US00500.
XX
PR   24-JAN-1990;   90US-0468736.
XX
PA   (BUCK/) BUCKLEY D I.
XX
PI   Buckley DI,  Habener JF,  Mallory JB,  Mojsov S;
XX
DR   WPI; 1991-252609/34.
XX
PT   New glucagon-like peptide-1 (GLP-1) analogues - have increased
PT   insulin-stimulating activity and/or resistance to degradation in
PT   vivo
XX
PS   Claim 7; Page 37; 50pp; English.
XX
CC   The peptides represented in AAR13420-27 are more powerful than glucagon
CC   in stimulating insulin release from islet cells and some of them are
CC   also more resistant to degradation in the plasma.  Doses are usually
```

```
CC   1 picog-1mg/kg, for the treatment of diabetes Type II.
CC   The last three amino acids may sequentially be omitted.
XX
SQ   Sequence   31 AA;

 AAR13420  Length: 31  January 22, 2004 18:02  Type: P  Check: 7361  ..

      1  HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID   AAR13422 standard; Protein; 31 AA.
XX
AC   AAR13422;
XX
DT   29-OCT-1991  (first entry)
XX
DE   Glucagon-like peptide-1 (A)8-GLP-1(7-37).
XX
KW   Glucagon; insulin; diabetes; degradation; islet cells.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Modified-site   2
FT                   /label= D-Ala
XX
PN   WO9111457-A.
XX
PD   08-AUG-1991.
XX
PF   24-JAN-1991;   91WO-US00500.
XX
PR   24-JAN-1990;   90US-0468736.
XX
PA   (BUCK/) BUCKLEY D I.
XX
PI   Buckley DI,  Habener JF,  Mallory JB,  Mojsov S;
XX
DR   WPI; 1991-252609/34.
XX
PT   New glucagon-like peptide-1 (GLP-1) analogues - have increased
PT   insulin-stimulating activity and/or resistance to degradation in
PT   vivo
XX
PS   Claim 7; Page 37; 50pp; English.
XX
CC   The peptides represented in AAR13420-27 are more powerful than glucagon
CC   in stimulating insulin release from islet cells and some of them are
CC   also more resistant to degradation in the plasma.  Doses are usually
CC   1 picog-1mg/kg, for the treatment of diabetes Type II.
CC   The last three amino acids may sequentially be omitted.
XX
SQ   Sequence   31 AA;

 AAR13422  Length: 31  January 22, 2004 18:02  Type: P  Check: 7361  ..

      1  HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID   AAR13423 standard; Protein; 31 AA.
XX
AC   AAR13423;
XX
DT   29-OCT-1991  (first entry)
XX
DE   Glucagon-like peptide-1 (E)9-GLP-1(7-37).
XX
KW   Glucagon; insulin; diabetes; degradation; islet cells.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Modified-site   3
FT                   /label= D-Glu
XX
PN   WO9111457-A.
XX
PD   08-AUG-1991.
XX
PF   24-JAN-1991;   91WO-US00500.
XX
PR   24-JAN-1990;   90US-0468736.
XX
PA   (BUCK/) BUCKLEY D I.
XX
PI   Buckley DI,  Habener JF,  Mallory JB,  Mojsov S;
XX
DR   WPI; 1991-252609/34.
XX
PT   New glucagon-like peptide-1 (GLP-1) analogues - have increased
PT   insulin-stimulating activity and/or resistance to degradation in
PT   vivo
XX
PS   Claim 7; Page 37; 50pp; English.
XX
CC   The peptides represented in AAR13420-27 are more powerful than glucagon
CC   in stimulating insulin release from islet cells and some of them are
CC   also more resistant to degradation in the plasma.  Doses are usually
CC   1 picog-1mg/kg, for the treatment of diabetes Type II.
CC   The last three amino acids may sequentially be omitted.
XX
SQ   Sequence   31 AA;

 AAR13423  Length: 31  January 22, 2004 18:02  Type: P  Check: 7361  ..

      1  HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID   AAR42668 standard; peptide; 31 AA.
XX
AC   AAR42668;
XX
DT   25-MAR-2003  (updated)
DT   26-APR-1994  (first entry)
XX
DE   Glucagon-like peptide (GLP-1(7-37)).
XX
KW   Glucagon-like peptide; GLP; phospholipid;
KW   dioctanoyl-L-alpha-phosphatidylcholine; diabetes;
KW   dilauroyl-L-alpha-phosphatidylcholine; insulinotropic agent.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 31
FT                   /note= "Gly31 may be omitted, in which case the
FT                         C-terminal is amidated"
XX
PN   WO9318785-A1.
XX
PD   30-SEP-1993.
XX
PF   18-MAR-1993;   93WO-DK00098.
XX
PR   19-MAR-1992;   92DK-0000364.
XX
PA   (NOVO ) NOVO-NORDISK AS.
XX
PI   Kirk O,  Pridal L;
XX
DR   WPI; 1993-320450/40.
XX
PT   Medicament for treatment of diabetes - contains glucagon-like
PT   peptide and phospholipid for intranasal admin.
XX
PS   Claim 1; Page 18; 24pp; English.
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```
XX
CC   A medicament for intranasal admin. comprises this glucagon-like
CC   peptide (GLP) and a phospholipid, e.g. dioctanoyl-L-alpha-
CC   phosphatidylcholine, dilauroyl-L-alpha-phosphatidylcholine, etc.
CC   The medicament is used as an insulinotropic agent in the treatment
CC   of diabetes.  It has a very favourable absorption profile: absorption
CC   is slightly protracted and a constant plasma concn. of GLP is provided
CC   over an extended period.  In addn. the phospholipid exerts a
CC   stabilising effecxt on the peptide.
CC   (Updated on 25-MAR-2003 to correct PN field.)
XX
SQ   Sequence   31 AA;

 AAR42668  Length: 31  January 22, 2004 18:02  Type: P  Check: 7361  ..

       1  HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID   AAR45432 standard; protein; 37 AA.
XX
AC   AAR45432;
XX
DT   25-MAR-2003  (updated)
DT   27-JUN-1994  (first entry)
XX
DE   Glucagon-like peptide I derivative.
XX
KW   Insulinotropic; activity; enhancing insulin activity; treatment;
KW   Type II diabetes.
XX
OS   Synthetic.
XX
PN   WO9325579-A1.
XX
PD   23-DEC-1993.
XX
PF   14-APR-1993;   93WO-US03388.
XX
PR   15-JUN-1992;   92US-0899073.
XX
PA   (PFIZ ) PFIZER INC.
XX
PI   Andrews GC,  Daumy GO,  Francoeur ML,  Larson ER;
XX
DR   WPI; 1994-007457/01.
XX
PT   New derivs. of glucagon-like peptide 1 and insulinotropin - used for
PT   enhancing insulin action in a mammal, partic. by iontophoretic admin.
XX
PS   Claim 1; Page 19; 32pp; English.
XX
CC   The sequence is that of a derivative of glucagon-like peptide I
CC   which has insulinotropic activity and is useful for enhancing
CC   insulin action in a mammal, partic. for treating Type II diabetes
CC   (claimed). It is partic. suited for delivery to a mammal by
CC   ionophoresis.
CC   (Updated on 25-MAR-2003 to correct PN field.)
XX
SQ   Sequence   37 AA;

 AAR45432  Length: 37  January 22, 2004 18:02  Type: P  Check: 2897  ..

       1  HDEFERHAEG TFTSDVSSYL EGQAAKEFIA WLVKGRG

!!AA_SEQUENCE 1.0
ID   AAR45434 standard; protein; 31 AA.
XX
AC   AAR45434;
XX
DT   25-MAR-2003  (updated)
DT   27-JUN-1994  (first entry)
XX
DE   Insulinotropin derivative.
XX
KW   Insulinotropic; activity; enhancing insulin activity; treatment;
KW   Type II diabetes.
XX
OS   Synthetic.
XX
PN   WO9325579-A1.
XX
PD   23-DEC-1993.
XX
PF   14-APR-1993;   93WO-US03388.
XX
PR   15-JUN-1992;   92US-0899073.
XX
PA   (PFIZ ) PFIZER INC.
XX
PI   Andrews GC,  Daumy GO,  Francoeur ML,  Larson ER;
XX
DR   WPI; 1994-007457/01.
XX
PT   New derivs. of glucagon-like peptide 1 and insulinotropin - used for
PT   enhancing insulin action in a mammal, partic. by iontophoretic admin.
XX
PS   Claim 3; Page 20; 32pp; English.
XX
CC   The sequence is that of a derivative of insulinotropin which
CC   has insulinotropic activity and is useful for enhancing insulin
CC   action in a mammal, partic. for treating Type II diabetes
CC   (claimed). It is partic. suited for delivery to a mammal by
CC   ionophoresis.
CC   (Updated on 25-MAR-2003 to correct PN field.)
XX
SQ   Sequence   31 AA;

 AAR45434  Length: 31  January 22, 2004 18:02  Type: P  Check: 7361  ..

       1  HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID   AAR63245 standard; peptide; 37 AA.
XX
AC   AAR63245;
XX
DT   25-MAR-2003  (updated)
DT   01-MAY-1995  (first entry)
XX
DE   Glucagon-like peptide 1 (GLP-1) for use in treating NIDDM.
XX
KW   insulinotropic activity; GLP-1; glucagon-like protein 1; NIDDM;
KW   non-insulin dependent diabetes mellitus; insulintropin.
XX
OS   Synthetic.
XX
PN   EP619322-A2.
XX
PD   12-OCT-1994.
XX
PF   10-FEB-1994;   94EP-0300981.
XX
PR   07-APR-1993;   93US-0044133.
XX
PA   (PFIZ ) PFIZER INC.
PA   (SCIO-) SCIOS INC.
XX
PI   Danley DE,  Gelfand RA,  Geoghegan KF,  Kim Y,  Lambert WJ;
PI   Qi H,  Oih,  Hong Q,  Yesook K;
XX
DR   WPI; 1994-311774/39.
XX
PT   Treatment of non-insulin dependent diabetes mellitus - using a
PT   glucagon-like peptide 1 or deriv. with prolonged action for
PT   sustained glycaemic control
XX
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PS   Claim 2; Page 46; 70pp; English.
XX
CC   This peptide is glucagon-like peptide 1 (GLP-1). GLP-1 and its
CC   deriv.s are useful in the treatment of Non-Insulin Dependent
CC   Diabetes Mellitus (NIDDM). During processing in the pancreas and
CC   intestine, GLP-1 is converted to a 31 amino acid peptide having
CC   amino acids 7-37 of GLP-1 (AAR63245), alternatively referred to as
CC   insulinotropin. GLP-1(7-37) has insulinotropic activity, ie. it
CC   is able to stimulate, or cause to be stimulated, the synthesis
CC   of the hormone insulin. Other derivs. are shown in AAR63246-51. It
CC   has been discovered that prolonged plasma elevations of GLP-1,
CC   and related polypeptides, are necessary during the meal and beyond
CC   to achieve sustained glycemic control in patients with NIDDM. The
CC   invention provides a compsn. that has prolonged action after each
CC   administration.
CC   (Updated on 25-MAR-2003 to correct PN field.)
CC   (Updated on 25-MAR-2003 to correct PA field.)
XX
SQ   Sequence   37 AA;

 AAR63245  Length: 37  January 22, 2004 18:02  Type: P  Check: 2897  ..

       1  HDEFERHAEG TFTSDVSSYL EGQAAKEFIA WLVKGRG

!!AA_SEQUENCE 1.0
ID   AAR63246 standard; peptide; 31 AA.
XX
AC   AAR63246;
XX
DT   25-MAR-2003  (updated)
DT   02-MAY-1995  (first entry)
XX
DE   Insulinotropin (GLP-1(7-37)) for use in treating NIDDM.
XX
KW   insulinotropic activity; GLP-1; glucagon-like protein 1; NIDDM;
KW   non-insulin dependent diabetes mellitus; insulintropin.
XX
OS   Synthetic.
XX
PN   EP619322-A2.
XX
PD   12-OCT-1994.
XX
PF   10-FEB-1994;   94EP-0300981.
XX
PR   07-APR-1993;   93US-0044133.
XX
PA   (PFIZ ) PFIZER INC.
PA   (SCIO-) SCIOS INC.
XX
PI   Danley DE,  Gelfand RA,  Geoghegan KF,  Kim Y,  Lambert WJ;
PI   Qi H,  Oih,  Hong Q,  Yesook K;
XX
DR   WPI; 1994-311774/39.
XX
PT   Treatment of non-insulin dependent diabetes mellitus - using a
PT   glucagon-like peptide 1 or deriv. with prolonged action for
PT   sustained glycaemic control
XX
PS   Claim 2; Page 46; 70pp; English.
XX
CC   This peptide is GLP-1(7-37) [GLP = glucagon-like peptide]. GLP-1 and its
CC   deriv.s are useful in the treatment of Non-Insulin Dependent Diabetes
CC   Mellitus (NIDDM). During processing in the pancreas and intestine, GLP-1
CC   (AAR63245) is converted to a 31 amino acid peptide having amino acids
CC   7-37 of GLP-1, alternatively referred to as insulinotropin. GLP-1(7-37)
CC   has insulinotropic activity, ie. it is able to stimulate, or cause to be
CC   stimulated, the synthesis of the hormone insulin. Other derivs. are
CC   shown in AAR63247-51. It has been discovered that prolonged plasma
CC   elevations of GLP-1, and related polypeptides, are necessary during the
CC   meal and beyond to achieve sustained glycemic control in patients with
CC   NIDDM. The invention provides a compsn. that has prolonged action after
CC   each administration.
CC   (Updated on 25-MAR-2003 to correct PN field.)
CC   (Updated on 25-MAR-2003 to correct PA field.)
XX
SQ   Sequence   31 AA;

 AAR63246  Length: 31  January 22, 2004 18:02  Type: P  Check: 7361  ..

       1  HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID   AAR75885 standard; peptide; 31 AA.
XX
AC   AAR75885;
XX
DT   08-FEB-1996  (first entry)
XX
DE   Glucagon like peptide-1(7-36), (7-36)amide and (7-37).
XX
KW   Glucagon like peptide-1; GLP-1; (7-36); (7-36)amide; (7-37);
KW   type 2 diabetes; treatment.
XX
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Modified-site   36
FT                   /note= "may be amidated when Gly 31 is absent"
FT   Misc-difference 37
FT                   /note= "may be absent"
XX
PN   WO9517510-A1.
XX
PD   29-JUN-1995.
XX
PF   22-DEC-1994;   94WO-DK00487.
XX
PR   23-DEC-1993;   93DK-0001440.
XX
PA   (NOVO ) NOVO-NORDISK AS.
XX
PI   Bjorn SE,  Rasmussen JS,  Thim L;
XX
DR   WPI; 1995-240671/31.
XX
PT   Prodn. of glucagon-like peptide-1 (7-36) - using transformed
PT   bacteria contg. 2 or more consecutive DNA sequences coding for GLP-1
PT   (7-36)
XX
PS   Claim 1; Page 1; 27pp; English.
XX
CC   AAR75885 is the glucagon like peptide-1 (GLP-1) amino acids 7-36, the
CC   featured derivs. GLP-1(7-36)amide and GLP-1(7-37) are also given in
CC   the claims. The peptide and its derivs. can be used for the treatment
CC   of type 2 diabetes.
XX
SQ   Sequence   31 AA;

 AAR75885  Length: 31  January 22, 2004 18:02  Type: P  Check: 7361  ..

       1  HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID   AAR69065 standard; peptide; 31 AA.
XX
AC   AAR69065;
XX
DT   25-MAR-2003  (updated)
DT   23-AUG-1995  (first entry)
XX
DE   Glucagon like peptide 1 (GLP1) (7-36)-Gly.
XX
KW   Glucagon Like Peptide; GLP; transpeptidation; endopeptidase;
KW   trypsin; thrombin; cleavage.
XX
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```
OS   Synthetic.
XX
PN   WO9503405-A2.
XX
PD   02-FEB-1995.
XX
PF   19-JUL-1994;   94WO-US08125.
XX
PR   20-JUL-1993;   93US-0095162.
XX
PA   (BION-) BIONEBRASKA INC.
XX
PI   Henriksen D,  Manning S,  Partridge B,  Stout J,  Wagner FW;
XX
DR   WPI; 1995-075233/10.
XX
PT   Transpeptidation of recombinant polypeptides - using
PT   endopeptidase such as trypsin or thrombin to modify C-terminal
PT   residue.
XX
PS   Claim 34; Page 13; 69pp; English.
XX
CC   The naturally occurring sequence of Glucagon Like Peptide 1 (GLP1)
CC   is AAR69072. It is a 36 AA peptide that has been recombinantly
CC   produced but without a mechanism for providing for the amidation of
CC   the C-terminal Arg residue. Amidated recombinant GLP1 (7-36)NH2
CC   (AAR69063) was prepd. from a multicopy fusion protein contg. four
CC   copies of a modified truncated GLP peptide having AA residues 7-34
CC   of the native polypeptide and the terminal AA residues A-F-A at
CC   residues 35-37 (GLP1 (7-34)-A-F-A) (AAR69064). The recombinant GLP1 (7-
CC   34)-A-F-A can be transpeptidated to yield the modified recombinant
CC   native GLP1 (7-36)-NH2 (AAR69063) as follows. Trypsin was used to
CC   cleave the peptide at the Lys-Ala bond in the presence of either
CC   Gly-Arg-NH2 or Gly-Arg-Gly addition units so that the cleavage of
CC   the Ala-Phe-Arg leaving unit is followed by the addition of
CC   Gly-Arg-NH2 or Gly-Arg-Gly to the core GLP1 (7-34) to yield either
CC    amidated 7-36 GLP1-NH2 or GLP1 7-36 with a terminal Gly (AAR69065).
CC   (Updated on 25-MAR-2003 to correct PN field.)
XX
SQ   Sequence   31 AA;

 AAR69065  Length: 31  January 22, 2004 18:02  Type: P  Check: 7361  ..

      1  HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID   AAR69076 standard; peptide; 37 AA.
XX
AC   AAR69076;
XX
DT   25-MAR-2003  (updated)
DT   23-AUG-1995  (first entry)
XX
DE   Glucagon like peptide 1 (GLP1) (1-37).
XX
KW   Glucagon Like Peptide; GLP; transpeptidation; endopeptidase;
KW   trypsin; thrombin; cleavage.
XX
OS   Synthetic.
XX
PN   WO9503405-A2.
XX
PD   02-FEB-1995.
XX
PF   19-JUL-1994;   94WO-US08125.
XX
PR   20-JUL-1993;   93US-0095162.
XX
PA   (BION-) BIONEBRASKA INC.
XX
PI   Henriksen D,  Manning S,  Partridge B,  Stout J,  Wagner FW;
XX
DR   WPI; 1995-075233/10.
XX
PT   Transpeptidation of recombinant polypeptides - using
PT   endopeptidase such as trypsin or thrombin to modify C-terminal
PT   residue.
XX
PS   Example; Page 59; 69pp; English.
XX
CC   The naturally occurring sequence of Glucagon Like Peptide 1 (GLP1)
CC   is AAR69072. AAR69076 does not seem to be referred to in the patent
CC   application. it is described in the sequence listings as GLP
CC   (1-37).
CC   (Updated on 25-MAR-2003 to correct PN field.)
XX
SQ   Sequence   37 AA;

 AAR69076  Length: 37  January 22, 2004 18:02  Type: P  Check: 2897  ..

      1  HDEFERHAEG TFTSDVSSYL EGQAAKEFIA WLVKGRG

!!AA_SEQUENCE 1.0
ID   AAW03851 standard; peptide; 31 AA.
XX
AC   AAW03851;
XX
DT   25-MAR-2003  (updated)
DT   14-APR-1997  (first entry)
XX
DE   Glucagon like peptide 1 (7-37) analogue D-His7.
XX
KW   Human; glucagon like peptide; GLP-1; analogue; stimulation;
KW   pancreas; insulin; islet cell; treatment; type II diabetes;
KW   degradation; resistant.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 1
FT                   /note= "D-form residue"
XX
PN   US5545618-A.
XX
PD   13-AUG-1996.
XX
PF   10-DEC-1993;   93US-0165516.
XX
PR   20-SEP-1991;   91US-0762768.
PR   24-JAN-1990;   90US-0468736.
PR   10-DEC-1993;   93US-0165516.
XX
PA   (BUCK/) BUCKLEY D I.
PA   (HABE/) HABENER J F.
PA   (MALL/) MALLORY J B.
PA   (MOJS/) MOJSOV S.
XX
PI   Buckley DI,  Habener JF,  Mallory JB,  Mojsov S;
XX
DR   WPI; 1996-383697/38.
XX
PT   New modified glucagon-like peptide I fragments - have higher
PT   activity than glucagon or have improved plasma stability, useful for
PT   treating type II diabetes
XX
PS   Claim 14; page -; 16pp; English.
XX
CC   The present peptide is a human glucagon like peptide 1 (GLP-1)
CC   analogue, which is useful for stimulating insulin release from
CC   pancreatic islet cells, especially in the treatment of type II
CC   diabetes at doses of 1 pg/kg to 1 mg/kg. This peptide has better
CC   resistance to degradation in plasma than GLP-1(7-37), and has a
CC   higher activity than glucagon, as exemplified by the results of an
CC   adenylate cyclase assay where the peptide had an ED50 of 1.1 nM,
CC   compared to 0.16 nM for GLP-1(7-37) and 80 nM for glucagon.
CC   (Updated on 25-MAR-2003 to correct PF field.)
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XX
SQ   Sequence   31 AA;

 AAW03851  Length: 31  January 22, 2004 18:02  Type: P  Check: 7361  ..

      1  HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID   AAW03907 standard; peptide; 31 AA.
XX
AC   AAW03907;
XX
DT   25-MAR-2003  (updated)
DT   15-APR-1997  (first entry)
XX
DE   Glucagon like peptide 1 (7-37) analogue D-Lys34.
XX
KW   Human; glucagon like peptide; GLP-1; analogue; stimulation;
KW   pancreas; insulin; islet cell; treatment; type II diabetes.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 28
FT                   /note= "D-form residue"
FT   Misc-difference 29
FT                   /note= "optionally absent when Arg30 and Gly31 are
FT                    absent"
FT   Misc-difference 30
FT                   /note= "optionally absent when Gly31 is absent"
FT   Misc-difference 31
FT                   /note= "optionally absent"
XX
PN   US5545618-A.
XX
PD   13-AUG-1996.
XX
PF   10-DEC-1993;   93US-0165516.
XX
PR   20-SEP-1991;   91US-0762768.
PR   24-JAN-1990;   90US-0468736.
PR   10-DEC-1993;   93US-0165516.
XX
PA   (BUCK/) BUCKLEY D I.
PA   (HABE/) HABENER J F.
PA   (MALL/) MALLORY J B.
PA   (MOJS/) MOJSOV S.
XX
PI   Buckley DI,  Habener JF,  Mallory JB,  Mojsov S;
XX
DR   WPI; 1996-383697/38.
XX
PT   New modified glucagon-like peptide I fragments - have higher
PT   activity than glucagon or have improved plasma stability, useful for
PT   treating type II diabetes
XX
PS   Example 1; page -; 16pp; English.
XX
CC   The present peptide is a specific example of a claimed human
CC   glucagon like peptide 1 (GLP-1) analogue, which is useful for
CC   stimulating insulin release from pancreatic islet cells, especially
CC   in the treatment of type II diabetes at doses of 1 pg/kg to
CC   1 mg/kg.
CC   (Updated on 25-MAR-2003 to correct PF field.)
XX
SQ   Sequence   31 AA;

 AAW03907  Length: 31  January 22, 2004 18:02  Type: P  Check: 7361  ..

      1  HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID   AAW03929 standard; peptide; 31 AA.
XX
AC   AAW03929;
XX
DT   25-MAR-2003  (updated)
DT   15-APR-1997  (first entry)
XX
DE   Glucagon like peptide 1 (7-37) analogue D-Arg36.
XX
KW   Human; glucagon like peptide; GLP-1; analogue; stimulation;
KW   pancreas; insulin; islet cell; treatment; type II diabetes.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 30
FT                   /note= "D-form residue"
FT   Misc-difference 29
FT                   /note= "optionally absent when Arg30 and Gly31 are
FT                    absent"
FT   Misc-difference 30
FT                   /note= "optionally absent when Gly31 is absent"
FT   Misc-difference 31
FT                   /note= "optionally absent"
XX
PN   US5545618-A.
XX
PD   13-AUG-1996.
XX
PF   10-DEC-1993;   93US-0165516.
XX
PR   20-SEP-1991;   91US-0762768.
PR   24-JAN-1990;   90US-0468736.
PR   10-DEC-1993;   93US-0165516.
XX
PA   (BUCK/) BUCKLEY D I.
PA   (HABE/) HABENER J F.
PA   (MALL/) MALLORY J B.
PA   (MOJS/) MOJSOV S.
XX
PI   Buckley DI,  Habener JF,  Mallory JB,  Mojsov S;
XX
DR   WPI; 1996-383697/38.
XX
PT   New modified glucagon-like peptide I fragments - have higher
PT   activity than glucagon or have improved plasma stability, useful for
PT   treating type II diabetes
XX
PS   Example 1; page -; 16pp; English.
XX
CC   The present peptide is a specific example of a claimed human
CC   glucagon like peptide 1 (GLP-1) analogue, which is useful for
CC   stimulating insulin release from pancreatic islet cells, especially
CC   in the treatment of type II diabetes at doses of 1 pg/kg to
CC   1 mg/kg.
CC   (Updated on 25-MAR-2003 to correct PF field.)
XX
SQ   Sequence   31 AA;

 AAW03929  Length: 31  January 22, 2004 18:02  Type: P  Check: 7361  ..

      1  HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID   AAW03899 standard; peptide; 31 AA.
XX
AC   AAW03899;
XX
DT   25-MAR-2003  (updated)
DT   15-APR-1997  (first entry)
XX
DE   Glucagon like peptide 1 (7-37) analogue D-Lys26.
XX
KW   Human; glucagon like peptide; GLP-1; analogue; stimulation;
```

```
KW   pancreas; insulin; islet cell; treatment; type II diabetes.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 20
FT                   /note= "D-form residue"
FT   Misc-difference 29
FT                   /note= "optionally absent when Arg30 and Gly31 are
FT                    absent"
FT   Misc-difference 30
FT                   /note= "optionally absent when Gly31 is absent"
FT   Misc-difference 31
FT                   /note= "optionally absent"
XX
PN   US5545618-A.
XX
PD   13-AUG-1996.
XX
PF   10-DEC-1993;   93US-0165516.
XX
PR   20-SEP-1991;   91US-0762768.
PR   24-JAN-1990;   90US-0468736.
PR   10-DEC-1993;   93US-0165516.
XX
PA   (BUCK/) BUCKLEY D I.
PA   (HABE/) HABENER J F.
PA   (MALL/) MALLORY J B.
PA   (MOJS/) MOJSOV S.
XX
PI   Buckley DI,  Habener JF,  Mallory JB,  Mojsov S;
XX
DR   WPI; 1996-383697/38.
XX
PT   New modified glucagon-like peptide I fragments - have higher
PT   activity than glucagon or have improved plasma stability, useful for
PT   treating type II diabetes
XX
PS   Example 1; page -; 16pp; English.
XX
CC   The present peptide is a specific example of a claimed human
CC   glucagon like peptide 1 (GLP-1) analogue, which is useful for
CC   stimulating insulin release from pancreatic islet cells, especially
CC   in the treatment of type II diabetes at doses of 1 pg/kg to
CC   1 mg/kg.
CC   (Updated on 25-MAR-2003 to correct PF field.)
XX
SQ   Sequence   31 AA;

 AAW03899  Length: 31  January 22, 2004 18:02  Type: P  Check: 7361  ..

       1  HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID   AAW03865 standard; peptide; 31 AA.
XX
AC   AAW03865;
XX
DT   25-MAR-2003  (updated)
DT   15-APR-1997  (first entry)
XX
DE   Glucagon like peptide 1 (7-37) analogue N-formyl-(D-His/L-His7).
XX
KW   Human; glucagon like peptide; GLP-1; analogue; stimulation;
KW   pancreas; insulin; islet cell; treatment; type II diabetes.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   Modified-site   1
FT                   /note= "N-formyl-(D/L)-histidine"
FT   Misc-difference 29
FT                   /note= "optionally absent when Arg30 and Gly31 are
FT                    absent"
FT   Misc-difference 30
FT                   /note= "optionally absent when Gly31 is absent"
FT   Misc-difference 31
FT                   /note= "optionally absent"
XX
PN   US5545618-A.
XX
PD   13-AUG-1996.
XX
PF   10-DEC-1993;   93US-0165516.
XX
PR   20-SEP-1991;   91US-0762768.
PR   24-JAN-1990;   90US-0468736.
PR   10-DEC-1993;   93US-0165516.
XX
PA   (BUCK/) BUCKLEY D I.
PA   (HABE/) HABENER J F.
PA   (MALL/) MALLORY J B.
PA   (MOJS/) MOJSOV S.
XX
PI   Buckley DI,  Habener JF,  Mallory JB,  Mojsov S;
XX
DR   WPI; 1996-383697/38.
XX
PT   New modified glucagon-like peptide I fragments - have higher
PT   activity than glucagon or have improved plasma stability, useful for
PT   treating type II diabetes
XX
PS   Example 1; page -; 16pp; English.
XX
CC   The present peptide is a specific example of a claimed human
CC   glucagon like peptide 1 (GLP-1) analogue, which is useful for
CC   stimulating insulin release from pancreatic islet cells, especially
CC   in the treatment of type II diabetes at doses of 1 pg/kg to
CC   1 mg/kg.
CC   (Updated on 25-MAR-2003 to correct PF field.)
XX
SQ   Sequence   31 AA;

 AAW03865  Length: 31  January 22, 2004 18:02  Type: P  Check: 7361  ..

       1  HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID   AAW03866 standard; peptide; 31 AA.
XX
AC   AAW03866;
XX
DT   25-MAR-2003  (updated)
DT   15-APR-1997  (first entry)
XX
DE   Glucagon like peptide 1 (7-37) analogue N-acetyl-D-His7.
XX
KW   Human; glucagon like peptide; GLP-1; analogue; stimulation;
KW   pancreas; insulin; islet cell; treatment; type II diabetes.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   Modified-site   1
FT                   /note= "N-acetyl-D-histidine"
FT   Misc-difference 29
FT                   /note= "optionally absent when Arg30 and Gly31 are
FT                    absent"
FT   Misc-difference 30
FT                   /note= "optionally absent when Gly31 is absent"
FT   Misc-difference 31
FT                   /note= "optionally absent"
XX
PN   US5545618-A.
XX
PD   13-AUG-1996.
```

```
XX
PF   10-DEC-1993;   93US-0165516.
XX
PR   20-SEP-1991;   91US-0762768.
PR   24-JAN-1990;   90US-0468736.
PR   10-DEC-1993;   93US-0165516.
XX
PA   (BUCK/) BUCKLEY D I.
PA   (HABE/) HABENER J F.
PA   (MALL/) MALLORY J B.
PA   (MOJS/) MOJSOV S.
XX
PI   Buckley DI,  Habener JF,  Mallory JB,  Mojsov S;
XX
DR   WPI; 1996-383697/38.
XX
PT   New modified glucagon-like peptide I fragments - have higher
PT   activity than glucagon or have improved plasma stability, useful for
PT   treating type II diabetes
XX
PS   Example 1; page -; 16pp; English.
XX
CC   The present peptide is a specific example of a claimed human
CC   glucagon like peptide 1 (GLP-1) analogue, which is useful for
CC   stimulating insulin release from pancreatic islet cells, especially
CC   in the treatment of type II diabetes at doses of 1 pg/kg to
CC   1 mg/kg.
CC   (Updated on 25-MAR-2003 to correct PF field.)
XX
SQ   Sequence   31 AA;

 AAW03866  Length: 31  January 22, 2004 18:02  Type: P  Check: 7361  ..

       1  HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID   AAW03867 standard; peptide; 31 AA.
XX
AC   AAW03867;
XX
DT   25-MAR-2003  (updated)
DT   15-APR-1997  (first entry)
XX
DE   Glucagon like peptide 1 (7-37) analogue N-isopropyl-D-His7.
XX
KW   Human; glucagon like peptide; GLP-1; analogue; stimulation;
KW   pancreas; insulin; islet cell; treatment; type II diabetes.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   Modified-site   1
FT                   /note= "N-isopropyl-D-histidine"
FT   Misc-difference 29
FT                   /note= "optionally absent when Arg30 and Gly31 are
FT                        absent"
FT   Misc-difference 30
FT                   /note= "optionally absent when Gly31 is absent"
FT   Misc-difference 31
FT                   /note= "optionally absent"
XX
PN   US5545618-A.
XX
PD   13-AUG-1996.
XX
PF   10-DEC-1993;   93US-0165516.
XX
PR   20-SEP-1991;   91US-0762768.
PR   24-JAN-1990;   90US-0468736.
PR   10-DEC-1993;   93US-0165516.
XX
PA   (BUCK/) BUCKLEY D I.
PA   (HABE/) HABENER J F.
PA   (MALL/) MALLORY J B.
PA   (MOJS/) MOJSOV S.
XX
PI   Buckley DI,  Habener JF,  Mallory JB,  Mojsov S;
XX
DR   WPI; 1996-383697/38.
XX
PT   New modified glucagon-like peptide I fragments - have higher
PT   activity than glucagon or have improved plasma stability, useful for
PT   treating type II diabetes
XX
PS   Example 1; page -; 16pp; English.
XX
CC   The present peptide is a specific example of a claimed human
CC   glucagon like peptide 1 (GLP-1) analogue, which is useful for
CC   stimulating insulin release from pancreatic islet cells, especially
CC   in the treatment of type II diabetes at doses of 1 pg/kg to
CC   1 mg/kg.
CC   (Updated on 25-MAR-2003 to correct PF field.)
XX
SQ   Sequence   31 AA;

 AAW03867  Length: 31  January 22, 2004 18:02  Type: P  Check: 7361  ..

       1  HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID   AAW03853 standard; peptide; 31 AA.
XX
AC   AAW03853;
XX
DT   25-MAR-2003  (updated)
DT   14-APR-1997  (first entry)
XX
DE   Glucagon like peptide 1 (7-37) analogue N-isoproyl/N-acetyl His7.
XX
KW   Human; glucagon like peptide; GLP-1; analogue; stimulation;
KW   pancreas; insulin; islet cell; treatment; type II diabetes;
KW   degradation; resistant.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   Modified-site   1
FT                   /note= "N-isopropyl-histidine, or
FT                           N-acetyl-histidine"
XX
PN   US5545618-A.
XX
PD   13-AUG-1996.
XX
PF   10-DEC-1993;   93US-0165516.
XX
PR   20-SEP-1991;   91US-0762768.
PR   24-JAN-1990;   90US-0468736.
PR   10-DEC-1993;   93US-0165516.
XX
PA   (BUCK/) BUCKLEY D I.
PA   (HABE/) HABENER J F.
PA   (MALL/) MALLORY J B.
PA   (MOJS/) MOJSOV S.
XX
PI   Buckley DI,  Habener JF,  Mallory JB,  Mojsov S;
XX
DR   WPI; 1996-383697/38.
XX
PT   New modified glucagon-like peptide I fragments - have higher
PT   activity than glucagon or have improved plasma stability, useful for
PT   treating type II diabetes
XX
PS   Claim 14; page -; 16pp; English.
XX
CC   The present peptide is a human glucagon like peptide 1 (GLP-1)
```

```
CC   analogue, which is useful for stimulating insulin release from
CC   pancreatic islet cells, especially in the treatment of type II
CC   diabetes at doses of 1 pg/kg to 1 mg/kg. This peptide has better
CC   resistance to degradation in plasma than GLP-1(7-37), and has a
CC   higher activity than glucagon, as exemplified by the results of an
CC   adenylate cyclase assay where the peptide had an ED50 of 15.5 nM,
CC   compared to 0.16 nM for GLP-1(7-37) and 80 nM for glucagon.
CC   (Updated on 25-MAR-2003 to correct PF field.)
XX
SQ   Sequence   31 AA;

 AAW03853  Length: 31  January 22, 2004 18:02  Type: P  Check: 7361  ..

      1  HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID   AAW03854 standard; peptide; 31 AA.
XX
AC   AAW03854;
XX
DT   25-MAR-2003  (updated)
DT   14-APR-1997  (first entry)
XX
DE   Glucagon like peptide 1 (7-37) analogue D-Ala8.
XX
KW   Human; glucagon like peptide; GLP-1; analogue; stimulation;
KW   pancreas; insulin; islet cell; treatment; type II diabetes;
KW   degradation; resistant.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 2
FT                   /note= "D-form residue"
XX
PN   US5545618-A.
XX
PD   13-AUG-1996.
XX
PF   10-DEC-1993;   93US-0165516.
XX
PR   20-SEP-1991;   91US-0762768.
PR   24-JAN-1990;   90US-0468736.
PR   10-DEC-1993;   93US-0165516.
XX
PA   (BUCK/) BUCKLEY D I.
PA   (HABE/) HABENER J F.
PA   (MALL/) MALLORY J B.
PA   (MOJS/) MOJSOV S.
XX
PI   Buckley DI,  Habener JF,  Mallory JB,  Mojsov S;
XX
DR   WPI; 1996-383697/38.
XX
PT   New modified glucagon-like peptide I fragments - have higher
PT   activity than glucagon or have improved plasma stability, useful for
PT   treating type II diabetes
XX
PS   Claim 14; page -; 16pp; English.
XX
CC   The present peptide is a human glucagon like peptide 1 (GLP-1)
CC   analogue, which is useful for stimulating insulin release from
CC   pancreatic islet cells, especially in the treatment of type II
CC   diabetes at doses of 1 pg/kg to 1 mg/kg. This peptide has better
CC   resistance to degradation in plasma than GLP-1(7-37), and has a
CC   higher activity than glucagon, as exemplified by the results of an
CC   adenylate cyclase assay where the peptide had an ED50 of 0.40 nM,
CC   compared to 0.16 nM for GLP-1(7-37) and 80 nM for glucagon.
CC   (Updated on 25-MAR-2003 to correct PF field.)
XX
SQ   Sequence   31 AA;

 AAW03854  Length: 31  January 22, 2004 18:02  Type: P  Check: 7361  ..

      1  HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID   AAW03855 standard; peptide; 31 AA.
XX
AC   AAW03855;
XX
DT   25-MAR-2003  (updated)
DT   14-APR-1997  (first entry)
XX
DE   Glucagon like peptide 1 (7-37) analogue D-Glu9.
XX
KW   Human; glucagon like peptide; GLP-1; analogue; stimulation;
KW   pancreas; insulin; islet cell; treatment; type II diabetes;
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 3
FT                   /note= "D-form residue"
XX
PN   US5545618-A.
XX
PD   13-AUG-1996.
XX
PF   10-DEC-1993;   93US-0165516.
XX
PR   20-SEP-1991;   91US-0762768.
PR   24-JAN-1990;   90US-0468736.
PR   10-DEC-1993;   93US-0165516.
XX
PA   (BUCK/) BUCKLEY D I.
PA   (HABE/) HABENER J F.
PA   (MALL/) MALLORY J B.
PA   (MOJS/) MOJSOV S.
XX
PI   Buckley DI,  Habener JF,  Mallory JB,  Mojsov S;
XX
DR   WPI; 1996-383697/38.
XX
PT   New modified glucagon-like peptide I fragments - have higher
PT   activity than glucagon or have improved plasma stability, useful for
PT   treating type II diabetes
XX
PS   Claim 14; page -; 16pp; English.
XX
CC   The present peptide is a human glucagon like peptide 1 (GLP-1)
CC   analogue, which is useful for stimulating insulin release from
CC   pancreatic islet cells, especially in the treatment of type II
CC   diabetes at doses of 1 pg/kg to 1 mg/kg. This peptide has a
CC   higher activity than glucagon, as exemplified by the results of an
CC   adenylate cyclase assay where the peptide had an ED50 of 55.0 nM,
CC   compared to 0.16 nM for GLP-1(7-37) and 80 nM for glucagon.
CC   (Updated on 25-MAR-2003 to correct PF field.)
XX
SQ   Sequence   31 AA;

 AAW03855  Length: 31  January 22, 2004 18:02  Type: P  Check: 7361  ..

      1  HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID   AAW03873 standard; peptide; 31 AA.
XX
AC   AAW03873;
XX
DT   25-MAR-2003  (updated)
DT   15-APR-1997  (first entry)
XX
DE   Glucagon like peptide 1 (7-37) analogue Gly8.
XX
KW   Human; glucagon like peptide; GLP-1; analogue; stimulation;
```

```
KW   pancreas; insulin; islet cell; treatment; type II diabetes.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 2
FT                   /note= "wild type Ala substituted with Gly"
FT   Misc-difference 29
FT                   /note= "optionally absent when Arg30 and Gly31 are
FT                    absent"
FT   Misc-difference 30
FT                   /note= "optionally absent when Gly31 is absent"
FT   Misc-difference 31
FT                   /note= "optionally absent"
XX
PN   US5545618-A.
XX
PD   13-AUG-1996.
XX
PF   10-DEC-1993;   93US-0165516.
XX
PR   20-SEP-1991;   91US-0762768.
PR   24-JAN-1990;   90US-0468736.
PR   10-DEC-1993;   93US-0165516.
XX
PA   (BUCK/) BUCKLEY D I.
PA   (HABE/) HABENER J F.
PA   (MALL/) MALLORY J B.
PA   (MOJS/) MOJSOV S.
XX
PI   Buckley DI,  Habener JF,  Mallory JB,  Mojsov S;
XX
DR   WPI; 1996-383697/38.
XX
PT   New modified glucagon-like peptide I fragments - have higher
PT   activity than glucagon or have improved plasma stability, useful for
PT   treating type II diabetes
XX
PS   Example 1; page -; 16pp; English.
XX
CC   The present peptide is a specific example of a claimed human
CC   glucagon like peptide 1 (GLP-1) analogue, which is useful for
CC   stimulating insulin release from pancreatic islet cells, especially
CC   in the treatment of type II diabetes at doses of 1 pg/kg to
CC   1 mg/kg.
CC   (Updated on 25-MAR-2003 to correct PF field.)
XX
SQ   Sequence   31 AA;

 AAW03873  Length: 31  January 22, 2004 18:02  Type: P  Check: 7373  ..

       1  HGEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID   AAW22079 standard; Protein; 180 AA.
XX
AC   AAW22079;
XX
DT   03-FEB-1998  (first entry)
XX
DE   Rat preproglucagon.
XX
KW   Recombinant protein; expression; secretory cell line; rat;
KW   glucagon; peptide hormone; amidation; insulinoma; RIN; diabetes;
KW   gene therapy.
XX
OS   Rattus sp.
XX
PN   WO9726321-A2.
XX
PD   24-JUL-1997.
XX
PF   17-JAN-1997;   97WO-US00761.
XX
PR   15-OCT-1996;   96US-0028427.
PR   19-JAN-1996;   96US-0589028.
XX
PA   (BETA-) BETAGENE INC.
PA   (TEXA ) UNIV TEXAS SYSTEM.
XX
PI   Clark SA,  Halban PA,  Kruse F,  McGarry D,  Newgard CB;
PI   Normington KD, Quaade C,  Thigpen AE;
XX
DR   WPI; 1997-385326/35.
DR   N-PSDB; AAT75669.
XX
PT   Recombinant cell engineered to provide amylin to a mammal - useful
PT   to treat e.g. angiogenesis, anorexia, obesity, hypertension,
PT   osteoporosis etc.
XX
PS   Example 10; Page 282-283; 336pp; English.
XX
CC   This polypeptide comprises rat preproglucagon. The sequence can be
CC   expressed from a PCR-amplified cDNA clone (see AAT75669). RIN rat
CC   insulinoma cell lines expressing preproglucagon provided efficient
CC   amidation of a secreted, processed polypeptide. The invention
CC   provides methods for production of heterologous polypeptides using
CC   recombinantly engineered cell lines. Also described are methods of
CC   engineering cells for high level expression, methods of large-scale
CC   heterologous protein production, and methods for treatment of
CC   disease in vivo using viral delivery systems and recombinant cell
CC   lines.
XX
SQ   Sequence   180 AA;

AAW22079  Length: 180  January 22, 2004 18:02  Type: P  Check: 8911  ..

       1  MKTVYIVAGL FVMLVQGSWQ HAPQDTEENA RSFPASQTEP LEDPDQINED

      51  KRHSQGTFTS DYSKYLDSRR AQDFVQWLMN TKRNRNNIAK RHDEFERHAE

     101  GTFTSDVSSY LEGQAAKEFI AWLVKGRGER DFPEEVAIAE ELGRRHADGS

     151  FSDEMNTILD NLATRDFINW LIQTKITDKK

!!AA_SEQUENCE 1.0
ID   AAW22080 standard; Protein; 180 AA.
XX
AC   AAW22080;
XX
DT   03-FEB-1998  (first entry)
XX
DE   Human preproglucagon.
XX
KW   Recombinant protein; expression; secretory cell line; rat;
KW   glucagon; peptide hormone; amidation; insulinoma; RIN; diabetes;
KW   gene therapy.
XX
OS   Homo sapiens.
XX
PN   WO9726321-A2.
XX
PD   24-JUL-1997.
XX
PF   17-JAN-1997;   97WO-US00761.
XX
PR   15-OCT-1996;   96US-0028427.
PR   19-JAN-1996;   96US-0589028.
XX
PA   (BETA-) BETAGENE INC.
PA   (TEXA ) UNIV TEXAS SYSTEM.
XX
PI   Clark SA,  Halban PA,  Kruse F,  McGarry D,  Newgard CB;
PI   Normington KD, Quaade C,  Thigpen AE;
XX
DR   WPI; 1997-385326/35.
```

DR N-PSDB; AAT75672.
XX
PT Recombinant cell engineered to provide amylin to a mammal - useful
PT to treat e.g. angiogenesis, anorexia, obesity, hypertension,
PT osteoporosis etc.
XX
PS Example 10; Page 284-285; 336pp; English.
XX
CC This polypeptide comprises human preproglucagon. The sequence can
CC be expressed from a PCR-amplified cDNA clone (see AAT75672). RIN rat
CC insulinoma cell lines expressing preproglucagon provided efficient
CC amidation of a secreted, processed polypeptide. The invention
CC provides methods for production of heterologous polypeptides using
CC recombinantly engineered cell lines. Also described are methods of
CC engineering cells for high level expression, methods of large-scale
CC heterologous protein production, and methods for treatment of
CC disease in vivo using viral delivery systems and recombinant cell
CC lines.
XX
SQ Sequence 180 AA;

AAW22080 Length: 180 January 22, 2004 18:02 Type: P Check: 9748 ..

1 MKSIYFVAGL FVMLVQGSWQ RSLQDTEEKS RSFSASQADP LSDPDQMNED

51 KRHSQGTFTS DYSKYLDSRR AQDFVQWLMN TKRNRNNIAK RHDEFERHAE

101 GTFTSDVSSY LEGQAAKEFI AWLVKGRGRR DFPEEVAIVE ELGRRHADGS

151 FSDEMNTILD NLAARDFINW LIQTKITDRK

!!AA_SEQUENCE 1.0
ID AAW22081 standard; Protein; 180 AA.
XX
AC AAW22081;
XX
DT 03-FEB-1998 (first entry)
XX
DE Human preproglucagon mutant (R52A).
XX
KW Recombinant protein; expression; secretory cell line; rat;
KW glucagon; peptide hormone; amidation; insulinoma; RIN; diabetes;
KW gene therapy.
XX
OS Homo sapiens.
OS Synthetic.
XX
PN WO9726321-A2.
XX
PD 24-JUL-1997.
XX
PF 17-JAN-1997; 97WO-US00761.
XX
PR 15-OCT-1996; 96US-0028427.
PR 19-JAN-1996; 96US-0589028.
XX
PA (BETA-) BETAGENE INC.
PA (TEXA) UNIV TEXAS SYSTEM.
XX
PI Clark SA, Halban PA, Kruse F, McGarry D, Newgard CB;
PI Normington KD, Quaade C, Thigpen AE;
XX
DR WPI; 1997-385326/35.
DR N-PSDB; AAT22081.
XX
PT Recombinant cell engineered to provide amylin to a mammal - useful
PT to treat e.g. angiogenesis, anorexia, obesity, hypertension,
PT osteoporosis etc.
XX
PS Example 10; Page 286-287; 336pp; English.
XX
CC This polypeptide comprises an Arg52Ala mutant of human
CC preproglucagon. The sequence can be expressed from a PCR-
CC amplified mutated cDNA clone (see AAT75673). RIN rat insulinoma
CC cell lines expressing preproglucagon provided efficient amidation
CC of a secreted, processed polypeptide. The invention provides
CC methods for production of heterologous polypeptides using
CC recombinantly engineered cell lines. Also described are methods of
CC engineering cells for high level expression, methods of large-scale
CC heterologous protein production, and methods for treatment of
CC disease in vivo using viral delivery systems and recombinant cell
CC lines.
XX
SQ Sequence 180 AA;

AAW22081 Length: 180 January 22, 2004 18:02 Type: P Check: 8864 ..

1 MKSIYFVAGL FVMLVQGSWQ RSLQDTEEKS RSFSASQADP LSDPDQMNED

51 KAHSQGTFTS DYSKYLDSRR AQDFVQWLMN TKRNRNNIAK RHDEFERHAE

101 GTFTSDVSSY LEGQAAKEFI AWLVKGRGRR DFPEEVAIVE ELGRRHADGS

151 FSDEMNTILD NLAARDFINW LIQTKITDRK

!!AA_SEQUENCE 1.0
ID AAW24389 standard; peptide; 31 AA.
XX
AC AAW24389;
XX
DT 14-JAN-1998 (first entry)
XX
DE Glucagon-like peptide GLP-1(7-37) Ala8 analogue.
XX
KW Diabetes; non-insulin dependent diabetes mellitus; NIDDM;
KW insulin dependent diabetes mellitus; IDDM; gene therapy;
KW glucagon-like peptide; GLP.
XX
OS Synthetic.
XX
PN WO9729180-A1.
XX
PD 14-AUG-1997.
XX
PF 06-FEB-1997; 97WO-US01978.
XX
PR 23-FEB-1996; 96GB-0003847.
PR 06-FEB-1996; 96US-0012111.
XX
PA (ELIL) LILLY & CO ELI.
XX
PI Borts TL, Broderick CL, Dimarchi RD, Grinnell BW;
PI Miller AR;
XX
DR WPI; 1997-415336/38.
DR N-PSDB; AAT77296.
XX
PT Gene therapy of type I and type II diabetes - by in vivo expression
PT of glucagon like peptide GLP-1(7-37) analogue
XX
PS Claim 4; Page 8; 31pp; English.
XX
CC This sequence represents an analogue of a glucagon-like peptide
CC GLP-1(7-37), where an alanine is present at the position
CC corresponding to position 8 of the peptide (position 2 of the sequence
CC shown here). It provides a means of delivering long term amounts of a
CC GLP-1(7-37)-based protein, which is useful in treating type I and type II
CC diabetes. A stable mammalian cell line, which is immunologically
CC isolated from the mammal's immune system, is transformed with a vector
CC expressing a protein of the above sequence. This transformed cell line is
CC then implanted into the individual needing treatment. Once implanted, the
CC GLP-1(7-37) analogue, in conjunction with high serum glucose levels,
CC causes pancreatic cells to produce insulin in non-insulin dependent
CC diabetes mellitus (NIDDM) and delays gastric emptying in both NIDDM and
CC insulin dependent diabetes mellitus (IDDM) patients. An expression vector
CC coding for a protein of the above sequence can also be directly injected

```
CC   into the mammal, such that the vector is incorporated into a cell and
CC   secretes the protein. This method overcomes the problems of the short
CC   serum half life of GLP-1(7-37), allowing delivery of effective long term
CC   amounts for diabetes treatment.
XX
SQ   Sequence   31 AA;

 AAW24389  Length: 31  January 22, 2004 18:02  Type: P  Check: 7361  ..

      1  HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID   AAW24390 standard; peptide; 31 AA.
XX
AC   AAW24390;
XX
DT   14-JAN-1998  (first entry)
XX
DE   Glucagon-like peptide GLP-1(7-37) Val8 analogue.
XX
KW   Diabetes; non-insulin dependent diabetes mellitus; NIDDM;
KW   insulin dependent diabetes mellitus; IDDM; gene therapy;
KW   glucagon-like peptide; GLP.
XX
OS   Synthetic.
XX
PN   WO9729180-A1.
XX
PD   14-AUG-1997.
XX
PF   06-FEB-1997;   97WO-US01978.
XX
PR   23-FEB-1996;   96GB-0003847.
PR   06-FEB-1996;   96US-0012111.
XX
PA   (ELIL ) LILLY & CO ELI.
XX
PI   Borts TL,  Broderick CL,  Dimarchi RD,  Grinnell BW;
PI   Miller AR;
XX
DR   WPI; 1997-415336/38.
DR   N-PSDB; AAT77297.
XX
PT   Gene therapy of type I and type II diabetes - by in vivo expression
PT   of glucagon like peptide GLP-1(7-37) analogue
XX
PS   Claim 5; Page 8; 31pp; English.
XX
CC   This sequence represents an analogue of a glucagon-like peptide
CC   GLP-1(7-37), where an valine is present at the position
CC   corresponding to position 8 of the peptide (position 2 of the sequence
CC   shown here). It provides a means of delivering long term amounts of a
CC   GLP-1(7-37)-based protein, which is useful in treating type I and type II
CC   diabetes. A stable mammalian cell line, which  is immunologically
CC   isolated from the mammal's immune system, is transformed with a vector
CC   expressing a protein of the above sequence. This transformed cell line is
CC   then implanted into the individual needing treatment. Once implanted, the
CC   GLP-1(7-37) analogue, in conjunction with high serum glucose levels,
CC   causes pancreatic cells to produce insulin in non-insulin dependent
CC   diabetes mellitus (NIDDM) and delays gastric emptying in both NIDDM and
CC   insulin dependent diabetes mellitus (IDDM) patients. An expression vector
CC   coding for a protein of the above sequence can also be directly injected
CC   into the mammal, such that the vector is incorporated into a cell and
CC   secretes the protein. This method overcomes the problems of the short
CC   serum half life of GLP-1(7-37), allowing delivery of effective long term
CC   amounts for diabetes treatment.
XX
SQ   Sequence   31 AA;

 AAW24390  Length: 31  January 22, 2004 18:02  Type: P  Check: 7403  ..

      1  HVEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID   AAW16384 standard; Protein; 180 AA.
XX
AC   AAW16384;
XX
DT   25-MAR-2003  (updated)
DT   01-OCT-1997  (first entry)
XX
DE   Rat prepro-glucagon.
XX
KW   Glucagon-like peptide-1(7-36); GLP-1; insulin secretagogue;
KW   insulinotropic hormone; type II diabetes mellitus; therapy.
XX
OS   Rattus sp.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1. .20
FT                   /label= Sig_peptide
FT   Peptide         21. .50
FT                   /label= NH2-peptide
FT   Cleavage-site   51. .52
FT                   /note= "proteolytic cleavage site"
FT   Peptide         53. .81
FT                   /label= Glucagon
FT   Cleavage-site   82. .83
FT                   /note= "proteolytic cleavage site"
FT   Peptide         84. .89
FT                   /label= IP-I
FT   Cleavage-site   90. .91
FT                   /note= "proteolytic cleavage site"
FT   Peptide         92. .128
FT                   /label= GLP-I
FT   Cleavage-site   129. .130
FT                   /note= "proteolytic cleavage site"
FT   Peptide         131. .143
FT                   /label= IP-II
FT   Cleavage-site   144. .145
FT                   /note= "proteolytic cleavage site"
FT   Peptide         146. .178
FT                   /label= GLP-II
FT   Cleavage-site   179. .180
FT                   /note= "proteolytic cleavage site"
XX
PN   US5614492-A.
XX
PD   25-MAR-1997.
XX
PF   23-NOV-1993;   93US-0156800.
XX
PR   05-SEP-1991;   91US-0756215.
PR   05-MAY-1986;   86US-0859928.
PR   26-JAN-1988;   88US-0148517.
PR   01-JUN-1990;   90US-0532111.
PR   23-NOV-1993;   93US-0156800.
XX
PA   (GEHO ) GEN HOSPITAL CORP.
XX
PI   Habener JF;
XX
DR   WPI; 1997-201513/18.
DR   N-PSDB; AAT73216.
XX
PT   Glucagon-like peptide-1 fragment comprising amino acids 7-36 -
PT   useful for enhancing insulin production in pancreatic islet cells,
PT   especially for treating type II diabetes mellitus
XX
PS   Disclosure; Fig 1-1A; 37pp; English.
XX
CC   Rat preproglucagon (AAW16384) is processed by proteolytic cleavage to
CC   glucagon, glucagon-like peptide-1 (GLP-1) and GLP-2.  A peptide
CC   fragment of GLP-1, GLP-1(7-36) (see also AAW16363), has been shown to
CC   possess hormonal activity and can be used as an insulin
CC   secretagogue and for the treatment of type II diabetes mellitus.
```

```
CC   (Updated on 25-MAR-2003 to correct PF field.)
XX
SQ   Sequence   180 AA;

AAW16384  Length: 180  January 22, 2004 18:02  Type: P  Check: 8962  ..

       1  MKTVYIVAGL FVMLVQGSWQ HAPQDTEENA RSFPASQTEP LEDPDQINED

      51  KRHSQGTFTS DYSKYLDSRR AQDFVQWLMN NKRNRNNIAK RHDEFERHAE

     101  GTFTSDVSSY LEGQAAKEFI AWLVKGRGRR DFPEEVAIAE ELGRRHADGS

     151  FSDEMNTILD NLATRDFINW LIQTKITDKK

!!AA_SEQUENCE 1.0
ID   AAW63287 standard; peptide; 31 AA.
XX
AC   AAW63287;
XX
DT   29-SEP-1998  (first entry)
XX
DE   Glucagon-like peptide-1 (7-37).
XX
KW   GLP-1; glucagon-like peptide; obesity.
XX
OS   Homo sapiens.
XX
PN   WO9819698-A1.
XX
PD   14-MAY-1998.
XX
PF   04-NOV-1997;   97WO-US20114.
XX
PR   30-OCT-1997;   97US-0961405.
PR   05-NOV-1996;   96US-0030213.
XX
PA   (ELIL ) LILLY & CO ELI.
XX
PI   DiMarchi RD,  Efendic S;
XX
DR   WPI; 1998-286595/25.
XX
PT   Use of glucagon-like peptide-1 and analogues and derivatives - to
PT   reduce body weight, e.g., in treatment of obesity
XX
PS   Disclosure; Page 5; 42pp; English.
XX
CC   The patent describes a new method of reducing body weight which
CC   comprises administration of a composition comprising: (i) glucagon-
CC   like peptide-1 (GLP-1); (ii) a GLP-1 analogue; (iii) a GLP-1 derivative;
CC   (iv) an agonist of the GLP-1 receptor; (v) an agonist of the GLP-1
CC   signal transduction cascade; (vi) a compound which stimulates synthesis
CC   of endogenous GLP-1; (vii) a compound that stimulates release of
CC   endogenous GLP-1; or (viii) a salt of a material described in (i)-(vii).
CC   The method may be used for treatment of obesity. The present sequence,
CC   GLP-1 (7-37), represents a preferred GLP-1 compound which can be used
CC   in the method.
XX
SQ   Sequence   31 AA;

 AAW63287  Length: 31  January 22, 2004 18:02  Type: P  Check: 7361  ..

       1  HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID   AAW63289 standard; peptide; 31 AA.
XX
AC   AAW63289;
XX
DT   29-SEP-1998  (first entry)
XX
DE   Val8-Glucagon-like peptide-1 (7-37)-OH.
XX
KW   GLP-1; glucagon-like peptide; obesity.
XX
OS   Synthetic.
XX
PN   WO9819698-A1.
XX
PD   14-MAY-1998.
XX
PF   04-NOV-1997;   97WO-US20114.
XX
PR   30-OCT-1997;   97US-0961405.
PR   05-NOV-1996;   96US-0030213.
XX
PA   (ELIL ) LILLY & CO ELI.
XX
PI   DiMarchi RD,  Efendic S;
XX
DR   WPI; 1998-286595/25.
XX
PT   Use of glucagon-like peptide-1 and analogues and derivatives - to
PT   reduce body weight, e.g., in treatment of obesity
XX
PS   Claim 6; Page 18; 42pp; English.
XX
CC   The patent describes a new method of reducing body weight which
CC   comprises administration of a composition comprising: (i) glucagon-
CC   like peptide-1 (GLP-1); (ii) a GLP-1 analogue; (iii) a GLP-1 derivative;
CC   (iv) an agonist of the GLP-1 receptor; (v) an agonist of the GLP-1
CC   signal transduction cascade; (vi) a compound which stimulates synthesis
CC   of endogenous GLP-1; (vii) a compound that stimulates release of
CC   endogenous GLP-1; or (viii) a salt of a material described in (i)-(vii).
CC   The method may be used for treatment of obesity. The present sequence,
CC   Val8-GLP-1 (7-37), represents a preferred GLP-1 compound which can be
CC   used in the method.
XX
SQ   Sequence   31 AA;

 AAW63289  Length: 31  January 22, 2004 18:02  Type: P  Check: 7403  ..

       1  HVEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID   AAW63180 standard; peptide; 45 AA.
XX
AC   AAW63180;
XX
DT   16-SEP-1998  (first entry)
XX
DE   GLP-1(1-45).
XX
KW   Glucagon-like peptide-1; GLP-1; diabetes; lipophilic; tetradecanoyl;
KW   carboxynonadecanoyl; deoxycholoyl; choloyl; lithocholoyl.
XX
OS   Homo sapiens.
XX
PN   WO9808871-A1.
XX
PD   05-MAR-1998.
XX
PF   22-AUG-1997;   97WO-DK00340.
XX
PR   20-DEC-1996;   96DK-0001470.
PR   30-AUG-1996;   96DK-0000931.
PR   08-NOV-1996;   96DK-0001259.
XX
PA   (NOVO ) NOVO-NORDISK AS.
XX
PI   Knudsen LB,  Nielsen PF,  Sorensen PO;
XX
DR   WPI; 1998-239721/21.
XX
PT   Glucagon-like peptide-1 derivatives which have lipophilic
PT   substituent - exhibit protracted profiles of action relative to
```

PT known glucagon-like peptide-1 compounds and are useful in
PT treatment of diabetes
XX
PS Claim 34; Page -; 76pp; English.
XX
CC New derivatives of glucagon-like peptide-1 (GLP-1) and its fragments
CC and their analogues are disclosed in which at least one amino acid
CC residue of the parent peptide has a lipophilic substituent attached
CC to it. The GLP-1 fragment is preferably GLP-1(A-C) where A is 1-7 and
CC C is 35-45. The lipophilic substituent is typically tetradecanoyl,
CC carboxynonadecanoyl, deoxycholoyl, choloyl or lithocholoyl, and it
CC is attached e.g. to the epsilon-amino group of a Lys residue in the
CC peptide. The present sequence represents a preferred parent GLP-1
CC fragment to which the lipophilic substituent is to be attached.
CC GLP-1 and its analogues and fragments may be used in treatment of
CC type 1 and type 2 diabetes: Prior art analogues exhibit a high
CC clearance rate from the body, which limits their usefulness. The
CC new lipophilically substituted compounds have a protracted profile
CC of action compared with known analogues, e.g. GLP-1(7-37).
CC (N.B. The present sequence is described by name in the patent
CC specification but is not explicitly shown. It is deduced from the
CC protein sequence shown in Swiss-Prot entry P01275 using information
CC given in the patent.)
XX
SQ Sequence 45 AA;

AAW63180 Length: 45 January 22, 2004 18:02 Type: P Check: 8034 ..

1 HDEFERHAEG TFTSDVSSYL EGQAAKEFIA WLVKGRGRRD FPEEV

!!AA_SEQUENCE 1.0
ID AAW63183 standard; peptide; 31 AA.
XX
AC AAW63183;
XX
DT 16-SEP-1998 (first entry)
XX
DE GLP-1(7-37).
XX
KW Glucagon-like peptide-1; GLP-1; diabetes; lipophilic; tetradecanoyl;
KW carboxynonadecanoyl; deoxycholoyl; choloyl; lithocholoyl.
XX
OS Homo sapiens.
XX
PN WO9808871-A1.
XX
PD 05-MAR-1998.
XX
PF 22-AUG-1997; 97WO-DK00340.
XX
PR 20-DEC-1996; 96DK-0001470.
PR 30-AUG-1996; 96DK-0000931.
PR 08-NOV-1996; 96DK-0001259.
XX
PA (NOVO) NOVO-NORDISK AS.
XX
PI Knudsen LB, Nielsen PF, Sorensen PO;
XX
DR WPI; 1998-239721/21.
XX
PT Glucagon-like peptide-1 derivatives which have lipophilic
PT substituent - exhibit protracted profiles of action relative to
PT known glucagon-like peptide-1 compounds and are useful in
PT treatment of diabetes
XX
PS Claim 36; Page -; 76pp; English.
XX
CC New derivatives of glucagon-like peptide-1 (GLP-1) and its fragments
CC and their analogues are disclosed in which at least one amino acid
CC residue of the parent peptide has a lipophilic substituent attached
CC to it. The GLP-1 fragment is preferably GLP-1(A-C) where A is 1-7 and
CC C is 35-45. The lipophilic substituent is typically tetradecanoyl,
CC carboxynonadecanoyl, deoxycholoyl, choloyl or lithocholoyl, and it
CC is attached e.g. to the epsilon-amino group of a Lys residue in the
CC peptide. The present sequence represents a preferred parent GLP-1
CC fragment to which the lipophilic substituent is to be attached.
CC GLP-1 and its analogues and fragments may be used in treatment of
CC type 1 and type 2 diabetes. Prior art analogues exhibit a high
CC clearance rate from the body, which limits their usefulness. The
CC new lipophilically substituted compounds have a protracted profile
CC of action compared with known analogues, e.g. GLP-1(7-37).
CC (N.B. The present sequence is described by name in the patent
CC specification but is not explicitly shown. It is deduced from the
CC protein sequence shown in Swiss-Prot entry P01275 using information
CC given in the patent.)
XX
SQ Sequence 31 AA;

AAW63183 Length: 31 January 22, 2004 18:02 Type: P Check: 7361 ..

1 HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID AAW63184 standard; peptide; 32 AA.
XX
AC AAW63184;
XX
DT 16-SEP-1998 (first entry)
XX
DE GLP-1(7-38).
XX
KW Glucagon-like peptide-1; GLP-1; diabetes; lipophilic; tetradecanoyl;
KW carboxynonadecanoyl; deoxycholoyl; choloyl; lithocholoyl.
XX
OS Homo sapiens.
XX
PN WO9808871-A1.
XX
PD 05-MAR-1998.
XX
PF 22-AUG-1997; 97WO-DK00340.
XX
PR 20-DEC-1996; 96DK-0001470.
PR 30-AUG-1996; 96DK-0000931.
PR 08-NOV-1996; 96DK-0001259.
XX
PA (NOVO) NOVO-NORDISK AS.
XX
PI Knudsen LB, Nielsen PF, Sorensen PO;
XX
DR WPI; 1998-239721/21.
XX
PT Glucagon-like peptide-1 derivatives which have lipophilic
PT substituent - exhibit protracted profiles of action relative to
PT known glucagon-like peptide-1 compounds and are useful in
PT treatment of diabetes
XX
PS Claim 36; Page -; 76pp; English.
XX
CC New derivatives of glucagon-like peptide-1 (GLP-1) and its fragments
CC and their analogues are disclosed in which at least one amino acid
CC residue of the parent peptide has a lipophilic substituent attached
CC to it. The GLP-1 fragment is preferably GLP-1(A-C) where A is 1-7 and
CC C is 35-45. The lipophilic substituent is typically tetradecanoyl,
CC carboxynonadecanoyl, deoxycholoyl, choloyl or lithocholoyl, and it
CC is attached e.g. to the epsilon-amino group of a Lys residue in the
CC peptide. The present sequence represents a preferred parent GLP-1
CC fragment to which the lipophilic substituent is to be attached.
CC GLP-1 and its analogues and fragments may be used in treatment of
CC type 1 and type 2 diabetes. Prior art analogues exhibit a high
CC clearance rate from the body, which limits their usefulness. The
CC new lipophilically substituted compounds have a protracted profile
CC of action compared with known analogues, e.g. GLP-1(7-37).
CC (N.B. The present sequence is described by name in the patent
CC specification but is not explicitly shown. It is deduced from the
CC protein sequence shown in Swiss-Prot entry P01275 using information

CC given in the patent.)
XX
SQ Sequence 32 AA;

AAW63184 Length: 32 January 22, 2004 18:02 Type: P Check: 9985 ..

1 HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR GR

!!AA_SEQUENCE 1.0
ID AAW63185 standard; peptide; 33 AA.
XX
AC AAW63185;
XX
DT 16-SEP-1998 (first entry)
XX
DE GLP-1(7-39).
XX
KW Glucagon-like peptide-1; GLP-1; diabetes; lipophilic; tetradecanoyl;
KW carboxynonadecanoyl; deoxycholoyl; choloyl; lithocholoyl.
XX
OS Homo sapiens.
XX
PN WO9808871-A1.
XX
PD 05-MAR-1998.
XX
PF 22-AUG-1997; 97WO-DK00340.
XX
PR 20-DEC-1996; 96DK-0001470.
PR 30-AUG-1996; 96DK-0000931.
PR 08-NOV-1996; 96DK-0001259.
XX
PA (NOVO) NOVO-NORDISK AS.
XX
PI Knudsen LB, Nielsen PF, Sorensen PO;
XX
DR WPI; 1998-239721/21.
XX
PT Glucagon-like peptide-1 derivatives which have lipophilic
PT substituent - exhibit protracted profiles of action relative to
PT known glucagon-like peptide-1 compounds and are useful in
PT treatment of diabetes
XX
PS Claim 36; Page -; 76pp; English.
XX
CC New derivatives of glucagon-like peptide-1 (GLP-1) and its fragments
CC and their analogues are disclosed in which at least one amino acid
CC residue of the parent peptide has a lipophilic substituent attached
CC to it. The GLP-1 fragment is preferably GLP-1(A-C) where A is 1-7 and
CC C is 35-45. The lipophilic substituent is typically tetradecanoyl,
CC carboxynonadecanoyl, deoxycholoyl, choloyl or lithocholoyl, and it
CC is attached e.g. to the epsilon-amino group of a Lys residue in the
CC peptide. The present sequence represents a preferred parent GLP-1
CC fragment to which the lipophilic substituent is to be attached.
CC GLP-1 and its analogues and fragments may be used in treatment of
CC type 1 and type 2 diabetes. Prior art analogues exhibit a high
CC clearance rate from the body, which limits their usefulness. The
CC new lipophilically substituted compounds have a protracted profile
CC of action compared with known analogues, e.g. GLP-1(7-37).
CC (N.B. The present sequence is described by name in the patent
CC specification but is not explicitly shown. It is deduced from the
CC protein sequence shown in Swiss-Prot entry P01275 using information
CC given in the patent.)
XX
SQ Sequence 33 AA;

AAW63185 Length: 33 January 22, 2004 18:02 Type: P Check: 2691 ..

1 HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR GRR

!!AA_SEQUENCE 1.0
ID AAW63186 standard; peptide; 34 AA.
XX
AC AAW63186;
XX
DT 16-SEP-1998 (first entry)
XX
DE GLP-1(7-40).
XX
KW Glucagon-like peptide-1; GLP-1; diabetes; lipophilic; tetradecanoyl;
KW carboxynonadecanoyl; deoxycholoyl; choloyl; lithocholoyl.
XX
OS Homo sapiens.
XX
PN WO9808871-A1.
XX
PD 05-MAR-1998.
XX
PF 22-AUG-1997; 97WO-DK00340.
XX
PR 20-DEC-1996; 96DK-0001470.
PR 30-AUG-1996; 96DK-0000931.
PR 08-NOV-1996; 96DK-0001259.
XX
PA (NOVO) NOVO-NORDISK AS.
XX
PI Knudsen LB, Nielsen PF, Sorensen PO;
XX
DR WPI; 1998-239721/21.
XX
PT Glucagon-like peptide-1 derivatives which have lipophilic
PT substituent - exhibit protracted profiles of action relative to
PT known glucagon-like peptide-1 compounds and are useful in
PT treatment of diabetes
XX
PS Claim 36; Page -; 76pp; English.
XX
CC New derivatives of glucagon-like peptide-1 (GLP-1) and its fragments
CC and their analogues are disclosed in which at least one amino acid
CC residue of the parent peptide has a lipophilic substituent attached
CC to it. The GLP-1 fragment is preferably GLP-1(A-C) where A is 1-7 and
CC C is 35-45. The lipophilic substituent is typically tetradecanoyl,
CC carboxynonadecanoyl, deoxycholoyl, choloyl or lithocholoyl, and it
CC is attached e.g. to the epsilon-amino group of a Lys residue in the
CC peptide. The present sequence represents a preferred parent GLP-1
CC fragment to which the lipophilic substituent is to be attached.
CC GLP-1 and its analogues and fragments may be used in treatment of
CC type 1 and type 2 diabetes. Prior art analogues exhibit a high
CC clearance rate from the body, which limits their usefulness. The
CC new lipophilically substituted compounds have a protracted profile
CC of action compared with known analogues, e.g. GLP-1(7-37).
CC (N.B. The present sequence is described by name in the patent
CC specification but is not explicitly shown. It is deduced from the
CC protein sequence shown in Swiss-Prot entry P01275 using information
CC given in the patent.)
XX
SQ Sequence 34 AA;

AAW63186 Length: 34 January 22, 2004 18:02 Type: P Check: 5003 ..

1 HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR GRRD

!!AA_SEQUENCE 1.0
ID AAW63187 standard; peptide; 35 AA.
XX
AC AAW63187;
XX
DT 16-SEP-1998 (first entry)
XX
DE GLP-1(7-41).
XX
KW Glucagon-like peptide-1; GLP-1; diabetes; lipophilic; tetradecanoyl;
KW carboxynonadecanoyl; deoxycholoyl; choloyl; lithocholoyl.
XX
OS Homo sapiens.
XX

PN WO9808871-A1.
XX
PD 05-MAR-1998.
XX
PF 22-AUG-1997; 97WO-DK00340.
XX
PR 20-DEC-1996; 96DK-0001470.
PR 30-AUG-1996; 96DK-0000931.
PR 08-NOV-1996; 96DK-0001259.
XX
PA (NOVO) NOVO-NORDISK AS.
XX
PI Knudsen LB, Nielsen PF, Sorensen PO;
XX
DR WPI; 1998-239721/21.
XX
PT Glucagon-like peptide-1 derivatives which have lipophilic
PT substituent - exhibit protracted profiles of action relative to
PT known glucagon-like peptide-1 compounds and are useful in
PT treatment of diabetes
XX
PS Claim 36; Page -; 76pp; English.
XX
CC New derivatives of glucagon-like peptide-1 (GLP-1) and its fragments
CC and their analogues are disclosed in which at least one amino acid
CC residue of the parent peptide has a lipophilic substituent attached
CC to it. The GLP-1 fragment is preferably GLP-1(A-C) where A is 1-7 and
CC C is 35-45. The lipophilic substituent is typically tetradecanoyl,
CC carboxynonadecanoyl, deoxycholoyl, choloyl or lithocholoyl, and it
CC is attached e.g. to the epsilon-amino group of a Lys residue in the
CC peptide. The present sequence represents a preferred parent GLP-1
CC fragment to which the lipophilic substituent is to be attached.
CC GLP-1 and its analogues and fragments may be used in treatment of
CC type 1 and type 2 diabetes. Prior art analogues exhibit a high
CC clearance rate from the body, which limits their usefulness. The
CC new lipophilically substituted compounds have a protracted profile
CC of action compared with known analogues, e.g. GLP-1(7-37).
CC (N.B. The present sequence is described by name in the patent
CC specification but is not explicitly shown. It is deduced from the
CC protein sequence shown in Swiss-Prot entry P01275 using information
CC given in the patent.)
XX
SQ Sequence 35 AA;

AAW63187 Length: 35 January 22, 2004 18:02 Type: P Check: 7453 ..

1 HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR GRRDF

!!AA_SEQUENCE 1.0
ID AAW63190 standard; peptide; 37 AA.
XX
AC AAW63190;
XX
DT 16-SEP-1998 (first entry)
XX
DE GLP-1(1-37).
XX
KW Glucagon-like peptide-1; GLP-1; diabetes; lipophilic; tetradecanoyl;
KW carboxynonadecanoyl; deoxycholoyl; choloyl; lithocholoyl.
XX
OS Homo sapiens.
XX
PN WO9808871-A1.
XX
PD 05-MAR-1998.
XX
PF 22-AUG-1997; 97WO-DK00340.
XX
PR 20-DEC-1996; 96DK-0001470.
PR 30-AUG-1996; 96DK-0000931.
PR 08-NOV-1996; 96DK-0001259.
XX
PA (NOVO) NOVO-NORDISK AS.
XX
PI Knudsen LB, Nielsen PF, Sorensen PO;
XX
DR WPI; 1998-239721/21.
XX
PT Glucagon-like peptide-1 derivatives which have lipophilic
PT substituent - exhibit protracted profiles of action relative to
PT known glucagon-like peptide-1 compounds and are useful in
PT treatment of diabetes
XX
PS Claim 37; Page -; 76pp; English.
XX
CC New derivatives of glucagon-like peptide-1 (GLP-1) and its fragments
CC and their analogues are disclosed in which at least one amino acid
CC residue of the parent peptide has a lipophilic substituent attached
CC to it. The GLP-1 fragment is preferably GLP-1(A-C) where A is 1-7 and
CC C is 35-45. The lipophilic substituent is typically tetradecanoyl,
CC carboxynonadecanoyl, deoxycholoyl, choloyl or lithocholoyl, and it
CC is attached e.g. to the epsilon-amino group of a Lys residue in the
CC peptide. The present sequence represents a preferred parent GLP-1
CC fragment to which the lipophilic substituent is to be attached.
CC GLP-1 and its analogues and fragments may be used in treatment of
CC type 1 and type 2 diabetes. Prior art analogues exhibit a high
CC clearance rate from the body, which limits their usefulness. The
CC new lipophilically substituted compounds have a protracted profile
CC of action compared with known analogues, e.g. GLP-1(7-37).
CC (N.B. The present sequence is described by name in the patent
CC specification but is not explicitly shown. It is deduced from the
CC protein sequence shown in Swiss-Prot entry P01275 using information
CC given in the patent.)
XX
SQ Sequence 37 AA;

AAW63190 Length: 37 January 22, 2004 18:02 Type: P Check: 2897 ..

1 HDEFERHAEG TFTSDVSSYL EGQAAKEFIA WLVKGRG

!!AA_SEQUENCE 1.0
ID AAW63191 standard; peptide; 38 AA.
XX
AC AAW63191;
XX
DT 16-SEP-1998 (first entry)
XX
DE GLP-1(1-38).
XX
KW Glucagon-like peptide-1; GLP-1; diabetes; lipophilic; tetradecanoyl;
KW carboxynonadecanoyl; deoxycholoyl; choloyl; lithocholoyl.
XX
OS Homo sapiens.
XX
PN WO9808871-A1.
XX
PD 05-MAR-1998.
XX
PF 22-AUG-1997; 97WO-DK00340.
XX
PR 20-DEC-1996; 96DK-0001470.
PR 30-AUG-1996; 96DK-0000931.
PR 08-NOV-1996; 96DK-0001259.
XX
PA (NOVO) NOVO-NORDISK AS.
XX
PI Knudsen LB, Nielsen PF, Sorensen PO;
XX
DR WPI; 1998-239721/21.
XX
PT Glucagon-like peptide-1 derivatives which have lipophilic
PT substituent - exhibit protracted profiles of action relative to
PT known glucagon-like peptide-1 compounds and are useful in
PT treatment of diabetes
XX
PS Claim 37; Page -; 76pp; English.

```
XX
CC   New derivatives of glucagon-like peptide-1 (GLP-1) and its fragments
CC   and their analogues are disclosed in which at least one amino acid
CC   residue of the parent peptide has a lipophilic substituent attached
CC   to it. The GLP-1 fragment is preferably GLP-1(A-C) where A is 1-7 and
CC   C is 35-45. The lipophilic substituent is typically tetradecanoyl,
CC   carboxynonadecanoyl, deoxycholoyl, choloyl or lithocholoyl, and it
CC   is attached e.g. to the epsilon-amino group of a Lys residue in the
CC   peptide. The present sequence represents a preferred parent GLP-1
CC   fragment to which the lipophilic substituent is to be attached.
CC   GLP-1 and its analogues and fragments may be used in treatment of
CC   type 1 and type 2 diabetes. Prior art analogues exhibit a high
CC   clearance rate from the body, which limits their usefulness. The
CC   new lipophilically substituted compounds have a protracted profile
CC   of action compared with known analogues, e.g. GLP-1(7-37).
CC   (N.B. The present sequence is described by name in the patent
CC   specification but is not explicitly shown. It is deduced from the
CC   protein sequence shown in Swiss-Prot entry P01275 using information
CC   given in the patent.)
XX
SQ   Sequence   38 AA;

 AAW63191  Length: 38  January 22, 2004 18:02  Type: P  Check: 6013  ..

       1  HDEFERHAEG TFTSDVSSYL EGQAAKEFIA WLVKGRGR

!!AA_SEQUENCE 1.0
ID   AAW63192 standard; peptide; 39 AA.
XX
AC   AAW63192;
XX
DT   16-SEP-1998  (first entry)
XX
DE   GLP-1(1-39).
XX
KW   Glucagon-like peptide-1; GLP-1; diabetes; lipophilic; tetradecanoyl;
KW   carboxynonadecanoyl; deoxycholoyl; choloyl; lithocholoyl.
XX
OS   Homo sapiens.
XX
PN   WO9808871-A1.
XX
PD   05-MAR-1998.
XX
PF   22-AUG-1997;   97WO-DK00340.
XX
PR   20-DEC-1996;   96DK-0001470.
PR   30-AUG-1996;   96DK-0000931.
PR   08-NOV-1996;   96DK-0001259.
XX
PA   (NOVO ) NOVO-NORDISK AS.
XX
PI   Knudsen LB,  Nielsen PF,  Sorensen PO;
XX
DR   WPI; 1998-239721/21.
XX
PT   Glucagon-like peptide-1 derivatives which have lipophilic
PT   substituent - exhibit protracted profiles of action relative to
PT   known glucagon-like peptide-1 compounds and are useful in
PT   treatment of diabetes
XX
PS   Claim 37; Page -; 76pp; English.
XX
CC   New derivatives of glucagon-like peptide-1 (GLP-1) and its fragments
CC   and their analogues are disclosed in which at least one amino acid
CC   residue of the parent peptide has a lipophilic substituent attached
CC   to it. The GLP-1 fragment is preferably GLP-1(A-C) where A is 1-7 and
CC   C is 35-45. The lipophilic substituent is typically tetradecanoyl,
CC   carboxynonadecanoyl, deoxycholoyl, choloyl or lithocholoyl, and it
CC   is attached e.g. to the epsilon-amino group of a Lys residue in the
CC   peptide. The present sequence represents a preferred parent GLP-1
CC   fragment to which the lipophilic substituent is to be attached.
CC   GLP-1 and its analogues and fragments may be used in treatment of
CC   type 1 and type 2 diabetes. Prior art analogues exhibit a high
CC   clearance rate from the body, which limits their usefulness. The
CC   new lipophilically substituted compounds have a protracted profile
CC   of action compared with known analogues, e.g. GLP-1(7-37).
CC   (N.B. The present sequence is described by name in the patent
CC   specification but is not explicitly shown. It is deduced from the
CC   protein sequence shown in Swiss-Prot entry P01275 using information
CC   given in the patent.)
XX
SQ   Sequence   39 AA;

 AAW63192  Length: 39  January 22, 2004 18:02  Type: P  Check: 7211  ..

       1  HDEFERHAEG TFTSDVSSYL EGQAAKEFIA WLVKGRGRR

!!AA_SEQUENCE 1.0
ID   AAW63193 standard; peptide; 40 AA.
XX
AC   AAW63193;
XX
DT   16-SEP-1998  (first entry)
XX
DE   GLP-1(1-40).
XX
KW   Glucagon-like peptide-1; GLP-1; diabetes; lipophilic; tetradecanoyl;
KW   carboxynonadecanoyl; deoxycholoyl; choloyl; lithocholoyl.
XX
OS   Homo sapiens.
XX
PN   WO9808871-A1.
XX
PD   05-MAR-1998.
XX
PF   22-AUG-1997;   97WO-DK00340.
XX
PR   20-DEC-1996;   96DK-0001470.
PR   30-AUG-1996;   96DK-0000931.
PR   08-NOV-1996;   96DK-0001259.
XX
PA   (NOVO ) NOVO-NORDISK AS.
XX
PI   Knudsen LB,  Nielsen PF,  Sorensen PO;
XX
DR   WPI; 1998-239721/21.
XX
PT   Glucagon-like peptide-1 derivatives which have lipophilic
PT   substituent - exhibit protracted profiles of action relative to
PT   known glucagon-like peptide-1 compounds and are useful in
PT   treatment of diabetes
XX
PS   Claim 37; Page -; 76pp; English.
XX
CC   New derivatives of glucagon-like peptide-1 (GLP-1) and its fragments
CC   and their analogues are disclosed in which at least one amino acid
CC   residue of the parent peptide has a lipophilic substituent attached
CC   to it. The GLP-1 fragment is preferably GLP-1(A-C) where A is 1-7 and
CC   C is 35-45. The lipophilic substituent is typically tetradecanoyl,
CC   carboxynonadecanoyl, deoxycholoyl, choloyl or lithocholoyl, and it
CC   is attached e.g. to the epsilon-amino group of a Lys residue in the
CC   peptide. The present sequence represents a preferred parent GLP-1
CC   fragment to which the lipophilic substituent is to be attached.
CC   GLP-1 and its analogues and fragments may be used in treatment of
CC   type 1 and type 2 diabetes. Prior art analogues exhibit a high
CC   clearance rate from the body, which limits their usefulness. The
CC   new lipophilically substituted compounds have a protracted profile
CC   of action compared with known analogues, e.g. GLP-1(7-37).
CC   (N.B. The present sequence is described by name in the patent
CC   specification but is not explicitly shown. It is deduced from the
CC   protein sequence shown in Swiss-Prot entry P01275 using information
CC   given in the patent.)
XX
SQ   Sequence   40 AA;
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AAW63193 Length: 40 January 22, 2004 18:02 Type: P Check: 1931 ..

1 HDEFERHAEG TFTSDVSSYL EGQAAKEFIA WLVKGRGRRD

```
!!AA_SEQUENCE 1.0
ID   AAW63194 standard; peptide; 41 AA.
XX
AC   AAW63194;
XX
DT   16-SEP-1998  (first entry)
XX
DE   GLP-1(1-41).
XX
KW   Glucagon-like peptide-1; GLP-1; diabetes; lipophilic; tetradecanoyl;
KW   carboxynonadecanoyl; deoxycholoyl; choloyl; lithocholoyl.
XX
OS   Homo sapiens.
XX
PN   WO9808871-A1.
XX
PD   05-MAR-1998.
XX
PF   22-AUG-1997;   97WO-DK00340.
XX
PR   20-DEC-1996;   96DK-0001470.
PR   30-AUG-1996;   96DK-0000931.
PR   08-NOV-1996;   96DK-0001259.
XX
PA   (NOVO ) NOVO-NORDISK AS.
XX
PI   Knudsen LB,  Nielsen PF,  Sorensen PO;
XX
DR   WPI; 1998-239721/21.
XX
PT   Glucagon-like peptide-1 derivatives which have lipophilic
PT   substituent - exhibit protracted profiles of action relative to
PT   known glucagon-like peptide-1 compounds and are useful in
PT   treatment of diabetes
XX
PS   Claim 37; Page -; 76pp; English.
XX
CC   New derivatives of glucagon-like peptide-1 (GLP-1) and its fragments
CC   and their analogues are disclosed in which at least one amino acid
CC   residue of the parent peptide has a lipophilic substituent attached
CC   to it. The GLP-1 fragment is preferably GLP-1(A-C) where A is 1-7 and
CC   C is 35-45. The lipophilic substituent is typically tetradecanoyl,
CC   carboxynonadecanoyl, deoxycholoyl, choloyl or lithocholoyl, and it
CC   is attached e.g. to the epsilon-amino group of a Lys residue in the
CC   peptide. The present sequence represents a preferred parent GLP-1
CC   fragment to which the lipophilic substituent is to be attached.
CC   GLP-1 and its analogues and fragments may be used in treatment of
CC   type 1 and type 2 diabetes. Prior art analogues exhibit a high
CC   clearance rate from the body, which limits their usefulness. The
CC   new lipophilically substituted compounds have a protracted profile
CC   of action compared with known analogues, e.g. GLP-1(7-37).
CC   (N.B. The present sequence is described by name in the patent
CC   specification but is not explicitly shown. It is deduced from the
CC   protein sequence shown in Swiss-Prot entry P01275 using information
CC   given in the patent.)
XX
SQ   Sequence   41 AA;
```

AAW63194 Length: 41 January 22, 2004 18:02 Type: P Check: 4801 ..

1 HDEFERHAEG TFTSDVSSYL EGQAAKEFIA WLVKGRGRRD F

```
!!AA_SEQUENCE 1.0
ID   AAW63195 standard; peptide; 31 AA.
XX
AC   AAW63195;
XX
DT   16-SEP-1998  (first entry)
XX
DE   GLP-1(7-37).
XX
KW   Glucagon-like peptide-1; GLP-1; diabetes; lipophilic; tetradecanoyl;
KW   carboxynonadecanoyl; deoxycholoyl; choloyl; lithocholoyl.
XX
OS   Synthetic.
XX
PN   WO9808871-A1.
XX
PD   05-MAR-1998.
XX
PF   22-AUG-1997;   97WO-DK00340.
XX
PR   20-DEC-1996;   96DK-0001470.
PR   30-AUG-1996;   96DK-0000931.
PR   08-NOV-1996;   96DK-0001259.
XX
PA   (NOVO ) NOVO-NORDISK AS.
XX
PI   Knudsen LB,  Nielsen PF,  Sorensen PO;
XX
DR   WPI; 1998-239721/21.
XX
PT   Glucagon-like peptide-1 derivatives which have lipophilic
PT   substituent - exhibit protracted profiles of action relative to
PT   known glucagon-like peptide-1 compounds and are useful in
PT   treatment of diabetes
XX
PS   Claim 41; Page -; 76pp; English.
XX
CC   New derivatives of glucagon-like peptide-1 (GLP-1) and its fragments
CC   and their analogues are disclosed in which at least one amino acid
CC   residue of the parent peptide has a lipophilic substituent attached
CC   to it. The GLP-1 fragment is preferably GLP-1(A-C) where A is 1-7 and
CC   C is 35-45. The lipophilic substituent is typically tetradecanoyl,
CC   carboxynonadecanoyl, deoxycholoyl, choloyl or lithocholoyl, and it
CC   is attached e.g. to the epsilon-amino group of a Lys residue in the
CC   peptide. The present sequence represents a preferred parent GLP-1
CC   analogue to which the lipophilic substituent is to be attached.
CC   GLP-1 and its analogues and fragments may be used in treatment of
CC   type 1 and type 2 diabetes. Prior art analogues exhibit a high
CC   clearance rate from the body, which limits their usefulness. The
CC   new lipophilically substituted compounds have a protracted profile
CC   of action compared with known analogues, e.g. GLP-1(7-37).
CC   (N.B. The present sequence is described by name in the patent
CC   specification but is not explicitly shown. It is deduced from the
CC   protein sequence shown in Swiss-Prot entry P01275 using information
CC   given in the patent.)
XX
SQ   Sequence   31 AA;
```

AAW63195 Length: 31 January 22, 2004 18:02 Type: P Check: 7361 ..

1 HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

```
!!AA_SEQUENCE 1.0
ID   AAW50902 standard; peptide; 31 AA.
XX
AC   AAW50902;
XX
DT   17-AUG-1998  (first entry)
XX
DE   Glucagon-like peptide-1 (7-37).
XX
KW   Glucagon-like peptide-1; GLP-1 (7-37); GLP-1 analogue; surgical trauma;
KW   stress; hormonal response; insulin resistance; catabolic reaction;
KW   human; incretin hormone.
XX
OS   Homo sapiens.
XX
PN   WO9808873-A1.
XX
PD   05-MAR-1998.
```

XX
PF 26-AUG-1997; 97WO-US15042.
XX
PR 21-AUG-1997; 97US-0024982.
PR 30-AUG-1996; 96US-0024982.
XX
PA (ELIL) LILLY & CO ELI.
XX
PI Efendic S;
XX
DR WPI; 1998-239722/21.
XX
PT Use of glucagon-like peptide-1 and analogues and their derivatives
PT - to attenuate post-surgical catabolic changes, insulin resistance
PT and hormonal responses to stress
XX
PS Claim 1; Page 7; 42pp; English.
XX
CC The present sequence represents glucagon-like peptide-1 (GLP-1 (7-37)),
CC which is used in the methods of the invention. The methods are: (1) for
CC attenuating post-surgical catabolic changes and insulin resistance,
CC comprising administering glucagon-like peptide-1 (GLP-1), a GLP-1
CC analogue, a GLP-1 derivative, or a salt of this compound; (2) for
CC attenuating post-surgical catabolic changes and hormonal responses to
CC stress, comprising administering a compound which exerts insulino-tropic
CC activity by interacting with the same receptor (or receptors) with which
CC GLP-1, GLP-1 analogues and GLP-1 derivatives interact in exerting their
CC insulino-tropic activity, and (3) for attenuating post-surgical catabolic
CC changes and hormonal responses to stress, comprising administering a
CC compound which enhances insulin sensitivity by interacting with the same
CC receptor (or receptors) with which GLP-1, GLP-1 analogues and GLP-1
CC derivatives interact to enhance insulin sensitivity. The processes are
CC useful for improving recovery after surgery by preventing the catabolic
CC reaction and insulin resistance caused by surgical trauma and
CC exacerbated by pre-operative fasting. GLP-1's short half-life, and hence
CC the need for continuous administration, are not disadvantages, as the
CC patient is usually hospitalised before surgery, and fluids are
CC continuously administered parenterally, before, during and after surgery.
XX
SQ Sequence 31 AA;

AAW50902 Length: 31 January 22, 2004 18:02 Type: P Check: 7361 ..

1 HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

ID AAY80306 standard; peptide; 31 AA.
XX
AC AAY80306;
XX
DT 20-MAR-2003 (updated)
DT 24-MAY-2000 (first entry)
XX
DE Glucagon peptide-1 (7-37) analogue #1.
XX
KW Glucagon-Like Peptide-1 (7-37) analogue; GLP-1(7-37); anorectic;
KW antidiabetic; diabetes; obesity; metabolic stability.
XX
OS Synthetic.
XX
FH Key Location/Qualifiers
FT Misc-difference 14
FT /note= "D-form residue"
FT Modified-site 31
FT /note= "C-terminal amide"
XX
PN FR2777283-A1.
XX
PD 15-OCT-1999.
XX
PF 10-APR-1998; 98FR-0004559.
XX
PR 10-APR-1998; 98FR-0004559.
XX
PA (ADIR) ADIR & CIE.
XX
PI Calas B, Grassy G, Chavanieu A, Sarrauste De Menthiere C, Renard P;
PI Pfeiffer B, Manechez D;
XX
DR WPI; 1999-608797/12.
XX
PT New peptide for treating obesity and diabetes, and with improved
PT metabolic stability -
XX
PS Claim 5; Page 31; 36pp; French.
XX
CC The invention relates to new Glucagon-Like Peptide-1 (7-37) (t(GLP-1))
CC analogues of which this sequence represents a specific example of the
CC peptide having the generic formula AAY80304 or AAY80305. The peptides
CC have anorectic and antidiabetic activity and are used for treating
CC diseases associated to t(GLP-1), preferably type I or non-insulin
CC dependent type II diabetes, obesity. The peptides have improved metabolic
CC stability thus providing a longer lasting action compared to the natural
CC peptides.
CC (Updated on 20-MAR-2003 to correct DR field.)
XX
SQ Sequence 31 AA;

AAY80306 Length: 31 January 22, 2004 18:02 Type: P Check: 7361 ..

1 HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

ID AAY42936 standard; peptide; 31 AA.
XX
AC AAY42936;
XX
DT 20-DEC-1999 (first entry)
XX
DE Glucagon-like peptide GLP-1 (7-37).
XX
KW Glucagon-like peptide; GLP-1; antidiabetic; anti-obesity;
KW insulinotropic; appetite suppressant.
XX
OS Homo sapiens.
XX
PN WO9943707-A1.
XX
PD 02-SEP-1999.
XX
PF 25-FEB-1999; 99WO-DK00085.
XX
PR 27-FEB-1998; 98DK-0000263.
PR 27-FEB-1998; 98DK-0000268.
PR 08-APR-1998; 98DK-0000508.
XX
PA (NOVO) NOVO-NORDISK AS.
XX
PI Knudsen LB, Huusfeldt PO, Nielsen PF, Madsen K;
XX
DR WPI; 1999-540561/45.
XX
PT New N-modified peptide derivatives, useful for treating diabetes,
PT insulin resistance and obesity -
XX
PS Disclosure; Page 1; 62pp; English.
XX
CC New glucagon-like peptide-1 (GLP-1) derivatives are disclosed which
CC comprise residues 7-45 of GLP-1 or a fragment thereof, preferably
CC residues 7-36, 7-37 or 7-38 or their analogues, in which (a) a
CC lipophilic substituent is attached to at least one amino acid and (b)
CC the N-terminal is substituted with a group containing an optionally
CC substituted 5- or 6-membered N-heterocycle, e.g. imidazolyl. The
CC compounds stimulate secretion of insulin, suppress secretion of
CC glucagon, suppress gastric motility and/or restore glucose compliance
CC to beta-cells. They are used to treat insulin-dependent or non-insulin-

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CC   dependent diabetes mellitus, insulin resistance and obesity. They have
CC   a longer-lasting action than GLP-1 derivatives that lack the lipophilic
CC   substituent. Some of them also exist as partially structured micelle-
CC   like aggregates, so have improved solubility and stability. The present
CC   sequence is a specifically preferred example of a GLP-1 analogue on
CC   which the derivatives are based.
XX
SQ   Sequence   31 AA;

 AAY42936  Length: 31  January 22, 2004 18:02  Type: P  Check: 7361  ..

      1  HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID   AAY27375 standard; peptide; 31 AA.
XX
AC   AAY27375;
XX
DT   26-NOV-1999  (first entry)
XX
DE   Glucagon-like peptide 1 (GLP-1) fragment (residues 7-37).
XX
KW   Glucagon; glucagon-like peptide 1; GLP-1; detergent; glycogenolytic;
KW   gluconeogenesis; insulin secretion; diabetes mellitus; obesity;
KW   spasmolytic; hypoglycemia.
XX
OS   Synthetic.
XX
PN   WO9947160-A1.
XX
PD   23-SEP-1999.
XX
PF   08-MAR-1999;   99WO-DK00115.
XX
PR   13-MAR-1998;   98EP-0610006.
PR   18-MAR-1998;   98US-0078422.
XX
PA   (NOVO ) NOVO-NORDISK AS.
XX
PI   Kaarsholm NC;
XX
DR   WPI; 1999-561858/47.
XX
PT   Aqueous solution of glucagon or glucagon-like peptide-1 stabilized with
PT   charged detergent, for treating diabetes or obesity  -
XX
PS   Examples; Page 5; 27pp; English.
XX
CC   The invention provides an aqueous solution that comprises: (i) at least
CC   one glucagon or glucagon-like peptide-1 (GLP-1), or their analogs or
CC   derivatives (I) and (ii) at least one detergent, other than dodecyl
CC   phosphocholine. The peptide (I) has at least two positive or negative
CC   charges or at least one charge of each sign. Glucagon is involved in
CC   glycogenolytic and gluconeogenesis processes (it also has a spasmolytic
CC   effect on smooth muscle) while GLP-1 promotes secretion of insulin and
CC   suppresses that of glucagon. The polar head of detergent interacts with
CC   charged side chains in (I) while the hydrophobic tail interacts with the
CC   hydrophobic patch in (I). The solution is used to treat (non-)insulin-
CC   dependent diabetes mellitus and obesity. Glucagon is also used in
CC   radiology as a spasmolytic and for treating hypoglycemia. The detergent
CC   stabilizes the solutions, which are available for immediate use and can
CC   be stored for a long time at 4-25plusoC. The solutions may have pH
CC   between 4 and 9, allowing selection of conditions that suppress chemical
CC   degradation. The detergents are made from natural materials so have
CC   better biological compatibility than known detergents. The present
CC   sequence represents a GLP-1 peptide fragment.
XX
SQ   Sequence   31 AA;

 AAY27375  Length: 31  January 22, 2004 18:02  Type: P  Check: 7361  ..

      1  HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID   AAY39772 standard; peptide; 31 AA.
XX
AC   AAY39772;
XX
DT   26-NOV-1999  (first entry)
XX
DE   Glucagon like peptide-1 (7-37).
XX
KW   Glucagon-like peptide-1; GLP-1; appetite suppression; human; diabetes;
KW   spontaneous food intake; therapy.
XX
OS   Homo sapiens.
XX
PN   WO9947161-A1.
XX
PD   23-SEP-1999.
XX
PF   16-MAR-1999;   99WO-US05571.
XX
PR   19-MAR-1998;   98US-0078544.
XX
PA   (BION-) BIONEBRASKA INC.
XX
PI   Goke B,  Beglinger C,  Coolidge TR;
XX
DR   WPI; 1999-561859/47.
XX
PT   New composition for controlling food intake especially in diabetes
PT   sufferers -
XX
PS   Claim 4; Page 22; 35pp; English.
XX
CC   This sequence represents a glucagon-like peptide-1 sequence used in the
CC   composition of the invention. The composition is for appetite
CC   suppression, and comprises a compound binding to a GLP-1 receptor and a
CC   pharmaceutical carrier. The composition can be administered to control
CC   appetite and/or reduce spontaneous food intake in humans, especially in
CC   humans with diabetes.
XX
SQ   Sequence   31 AA;

 AAY39772  Length: 31  January 22, 2004 18:02  Type: P  Check: 7361  ..

      1  HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID   AAY39774 standard; peptide; 37 AA.
XX
AC   AAY39774;
XX
DT   26-NOV-1999  (first entry)
XX
DE   Glucagon like peptide-1 (1-37).
XX
KW   Glucagon-like peptide-1; GLP-1; appetite suppression; human; diabetes;
KW   spontaneous food intake; therapy.
XX
OS   Homo sapiens.
XX
PN   WO9947161-A1.
XX
PD   23-SEP-1999.
XX
PF   16-MAR-1999;   99WO-US05571.
XX
PR   19-MAR-1998;   98US-0078544.
XX
PA   (BION-) BIONEBRASKA INC.
XX
PI   Goke B,  Beglinger C,  Coolidge TR;
XX
DR   WPI; 1999-561859/47.
```

XX
PT New composition for controlling food intake especially in diabetes
PT sufferers -
XX
PS Disclosure; Page 8; 35pp; English.
XX
CC This sequence represents a glucagon-like peptide-1 sequence used in the
CC composition of the invention. The composition is for appetite
CC suppression, and comprises a compound binding to a GLP-1 receptor and a
CC pharmaceutical carrier. The composition can be administered to control
CC appetite and/or reduce spontaneous food intake in humans, especially in
CC humans with diabetes.
XX
SQ Sequence 37 AA;

AAY39774 Length: 37 January 22, 2004 18:02 Type: P Check: 2897 ..

1 HDEFERHAEG TFTSDVSSYL EGQAAKEFIA WLVKGRG

!!AA_SEQUENCE 1.0
ID AAY39810 standard; peptide; 31 AA.
XX
AC AAY39810;
XX
DT 30-NOV-1999 (first entry)
XX
DE Glucagon-like peptide-1 (7-36).
XX
KW Glucagon-like peptide-1; GLP-1; insulin; pancreatic beta-type islet cell;
KW therapy; maturity onset diabetes; type II diabetes mellitus.
XX
OS Homo sapiens.
XX
PN US5958909-A.
XX
PD 28-SEP-1999.
XX
PF 20-NOV-1996; 96US-0749762.
XX
PR 26-JAN-1988; 88US-0148517.
PR 05-SEP-1991; 91US-0756215.
PR 23-NOV-1993; 93US-0156800.
PR 05-MAY-1986; 86US-0859928.
PR 01-JUN-1990; 90US-0532111.
XX
PA (GEHO) GEN HOSPITAL CORP.
XX
PI Habener JF;
XX
DR WPI; 1999-561064/47.
XX
PT Use of derivatives of glucagon-like peptide-1 for the treatment of
PT maturity onset (type II) diabetes mellitus -
XX
PS Claim 1; Column 33; 39pp; English.
XX
CC This sequence represents a glucagon-like peptide-1 sequence. The
CC invention relates to a method for enhancing the expression of insulin in
CC pancreatic beta-type islet cells using derivatives of glucagon-like
CC peptide-1 (GLP-1). The GLP-1 sequence may be useful for the
CC therapy or treatment of maturity onset (type II) diabetes mellitus.
XX
SQ Sequence 31 AA;

AAY39810 Length: 31 January 22, 2004 18:02 Type: P Check: 7361 ..

1 HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID AAY39812 standard; peptide; 180 AA.
XX
AC AAY39812;
XX
DT 30-NOV-1999 (first entry)
XX
DE Preproglucagon protein sequence.
XX
KW Glucagon-like peptide-1; GLP-1; insulin; pancreatic beta-type islet cell;
KW therapy; maturity onset diabetes; type II diabetes mellitus;
KW preproglucagon.
XX
OS Homo sapiens.
XX
PN US5958909-A.
XX
PD 28-SEP-1999.
XX
PF 20-NOV-1996; 96US-0749762.
XX
PR 26-JAN-1988; 88US-0148517.
PR 05-SEP-1991; 91US-0756215.
PR 23-NOV-1993; 93US-0156800.
PR 05-MAY-1986; 86US-0859928.
PR 01-JUN-1990; 90US-0532111.
XX
PA (GEHO) GEN HOSPITAL CORP.
XX
PI Habener JF;
XX
DR WPI; 1999-561064/47.
DR N-PSDB; AAZ20678.
XX
PT Use of derivatives of glucagon-like peptide-1 for the treatment of
PT maturity onset (type II) diabetes mellitus -
XX
PS Disclosure; Fig 1; 39pp; English.
XX
CC This sequence represents the preproglucagon protein sequence. The
CC invention relates to a method for enhancing the expression of insulin in
CC pancreatic beta-type islet cells using derivatives of glucagon-like
CC peptide-1 (GLP-1). The GLP-1 sequence may be useful for the
CC therapy or treatment of maturity onset (type II) diabetes mellitus.
XX
SQ Sequence 180 AA;

AAY39812 Length: 180 January 22, 2004 18:02 Type: P Check: 9106 ..

1 MKTVYIVAGL FVMLVQGSWQ HAPQDTEENA RSFPASQTEP LEDPDQMNED

51 KRHSQGTFTS DYSKYLDSRR AQDFVQWLMN TKRNRNNIAK RHDEFERHAE

101 GTFTSDVSSY LEGQAAKEFI AWLVKGRGRR DFPEEVAIAE ELGRRHADGS

151 FSDEMNTILD NLATRDFINW LIQTKITDKK

!!AA_SEQUENCE 1.0
ID AAY34199 standard; peptide; 31 AA.
XX
AC AAY34199;
XX
DT 16-NOV-1999 (first entry)
XX
DE GLP-1 mutant peptide, GLP-1(7-37).
XX
KW GLP-1; Glucagon-like peptide-1; human; type I diabetes; type II diabetes;
KW obesity; therapy; mutein.
XX
OS Homo sapiens.
OS Synthetic.
XX
PN WO9943341-A1.
XX
PD 02-SEP-1999.
XX
PF 25-FEB-1999; 99WO-DK00084.
XX

PR 27-FEB-1998; 98DK-0000268.
PR 27-FEB-1998; 98DK-0000272.
XX
PA (NOVO) NOVO-NORDISK AS.
XX
PI Knudsen LB, Huusfeldt PO, Nielsen PF, Kaarsholm NC, Olsen HB;
PI Bjorn SE;
XX
DR WPI; 1999-540500/45.
XX
PT Composition containing stabilized derivatives of glucagon-like
PT peptide-1 with high alpha-helix content, for treating diabetes and
PT obesity
XX
PS Claim 30; Page -; 63pp; English.
XX
CC This sequence represents a mutant of the human glucagon-like peptide-1
CC (GLP-1), and has a helix content (determined by circular dichroism at
CC 222 nm in water at 20-24 degrees C) over 25, preferably 25-50,% at
CC peptide concentration about 10 microM. The GLP-1 mutant can be used in a
CC pharmaceutical composition of the invention. The compositions are used to
CC treat diabetes (both type I and particularly type II) and/or obesity.
CC They have better solubility and/or stability (against endogenous
CC diaminopeptidyl peptidase) than parent peptides, with long persistence in
CC the plasma and retention of biological activity. They form partially
CC structured micelle-like aggregates in solution, with the helix content
CC practically independent of concentration.
CC NOTE: This sequence was created from the human GLP-1 sequence using
CC information given in the specification.
XX
SQ Sequence 31 AA;

AAY34199 Length: 31 January 22, 2004 18:02 Type: P Check: 7361 ..

1 HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID AAY34200 standard; peptide; 32 AA.
XX
AC AAY34200;
XX
DT 16-NOV-1999 (first entry)
XX
DE GLP-1 mutant peptide, GLP-1(7-38).
XX
KW GLP-1; Glucagon-like peptide-1; human; type I diabetes; type II diabetes;
KW obesity; therapy; mutein.
XX
OS Homo sapiens.
OS Synthetic.
XX
PN WO9943341-A1.
XX
PD 02-SEP-1999.
XX
PF 25-FEB-1999; 99WO-DK00084.
XX
PR 27-FEB-1998; 98DK-0000268.
PR 27-FEB-1998; 98DK-0000272.
XX
PA (NOVO) NOVO-NORDISK AS.
XX
PI Knudsen LB, Huusfeldt PO, Nielsen PF, Kaarsholm NC, Olsen HB;
PI Bjorn SE;
XX
DR WPI; 1999-540500/45.
XX
PT Composition containing stabilized derivatives of glucagon-like
PT peptide-1 with high alpha-helix content, for treating diabetes and
PT obesity
XX
PS Claim 30; Page -; 63pp; English.
XX
CC This sequence represents a mutant of the human glucagon-like peptide-1
CC (GLP-1), and has a helix content (determined by circular dichroism at
CC 222 nm in water at 20-24 degrees C) over 25, preferably 25-50,% at
CC peptide concentration about 10 microM. The GLP-1 mutant can be used in a
CC pharmaceutical composition of the invention. The compositions are used to
CC treat diabetes (both type I and particularly type II) and/or obesity.
CC They have better solubility and/or stability (against endogenous
CC diaminopeptidyl peptidase) than parent peptides, with long persistence in
CC the plasma and retention of biological activity. They form partially
CC structured micelle-like aggregates in solution, with the helix content
CC practically independent of concentration.
CC NOTE: This sequence was created from the human GLP-1 sequence using
CC information given in the specification.
XX
SQ Sequence 32 AA;

AAY34200 Length: 32 January 22, 2004 18:02 Type: P Check: 9985 ..

1 HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR GR

!!AA_SEQUENCE 1.0
ID AAY34201 standard; peptide; 33 AA.
XX
AC AAY34201;
XX
DT 16-NOV-1999 (first entry)
XX
DE GLP-1 mutant peptide, GLP-1(7-39).
XX
KW GLP-1; Glucagon-like peptide-1; human; type I diabetes; type II diabetes;
KW obesity; therapy; mutein.
XX
OS Homo sapiens.
OS Synthetic.
XX
PN WO9943341-A1.
XX
PD 02-SEP-1999.
XX
PF 25-FEB-1999; 99WO-DK00084.
XX
PR 27-FEB-1998; 98DK-0000268.
PR 27-FEB-1998; 98DK-0000272.
XX
PA (NOVO) NOVO-NORDISK AS.
XX
PI Knudsen LB, Huusfeldt PO, Nielsen PF, Kaarsholm NC, Olsen HB;
PI Bjorn SE;
XX
DR WPI; 1999-540500/45.
XX
PT Composition containing stabilized derivatives of glucagon-like
PT peptide-1 with high alpha-helix content, for treating diabetes and
PT obesity
XX
PS Claim 30; Page -; 63pp; English.
XX
CC This sequence represents a mutant of the human glucagon-like peptide-1
CC (GLP-1), and has a helix content (determined by circular dichroism at
CC 222 nm in water at 20-24 degrees C) over 25, preferably 25-50,% at
CC peptide concentration about 10 microM. The GLP-1 mutant can be used in a
CC pharmaceutical composition of the invention. The compositions are used to
CC treat diabetes (both type I and particularly type II) and/or obesity.
CC They have better solubility and/or stability (against endogenous
CC diaminopeptidyl peptidase) than parent peptides, with long persistence in
CC the plasma and retention of biological activity. They form partially
CC structured micelle-like aggregates in solution, with the helix content
CC practically independent of concentration.
CC NOTE: This sequence was created from the human GLP-1 sequence using
CC information given in the specification.
XX
SQ Sequence 33 AA;

AAY34201 Length: 33 January 22, 2004 18:02 Type: P Check: 2691 ..

1 HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR GRR

```
!!AA_SEQUENCE 1.0
ID   AAY34202 standard; peptide; 34 AA.
XX
AC   AAY34202;
XX
DT   16-NOV-1999  (first entry)
XX
DE   GLP-1 mutant peptide, GLP-1(7-40).
XX
KW   GLP-1; Glucagon-like peptide-1; human; type I diabetes; type II diabetes;
KW   obesity; therapy; mutein.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
PN   WO9943341-A1.
XX
PD   02-SEP-1999.
XX
PF   25-FEB-1999;   99WO-DK00084.
XX
PR   27-FEB-1998;   98DK-0000268.
PR   27-FEB-1998;   98DK-0000272.
XX
PA   (NOVO ) NOVO-NORDISK AS.
XX
PI   Knudsen LB,  Huusfeldt PO,  Nielsen PF,  Kaarsholm NC,  Olsen HB;
PI   Bjorn SE;
XX
DR   WPI; 1999-540500/45.
XX
PT   Composition containing stabilized derivatives of glucagon-like
PT   peptide-1 with high alpha-helix content, for treating diabetes and
PT   obesity
XX
PS   Claim 30; Page -; 63pp; English.
XX
CC   This sequence represents a mutant of the human glucagon-like peptide-1
CC   (GLP-1), and has a helix content (determined by circular dichroism at
CC   222 nm in water at 20-24 degrees C) over 25, preferably 25-50,% at
CC   peptide concentration about 10 microM. The GLP-1 mutant can be used in a
CC   pharmaceutical composition of the invention. The compositions are used to
CC   treat diabetes (both type I and particularly type II) and/or obesity.
CC   They have better solubility and/or stability (against endogenous
CC   diaminopeptidyl peptidase) than parent peptides, with long persistence in
CC   the plasma and retention of biological activity. They form partially
CC   structured micelle-like aggregates in solution, with the helix content
CC   practically independent of concentration.
CC   NOTE: This sequence was created from the human GLP-1 sequence using
CC   information given in the specification.
XX
SQ   Sequence   34 AA;
```

AAY34202 Length: 34 January 22, 2004 18:02 Type: P Check: 5003 ..

1 HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR GRRD

```
!!AA_SEQUENCE 1.0
ID   AAY34203 standard; peptide; 35 AA.
XX
AC   AAY34203;
XX
DT   16-NOV-1999  (first entry)
XX
DE   GLP-1 mutant peptide, GLP-1(7-41).
XX
KW   GLP-1; Glucagon-like peptide-1; human; type I diabetes; type II diabetes;
KW   obesity; therapy; mutein.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
PN   WO9943341-A1.
XX
PD   02-SEP-1999.
XX
PF   25-FEB-1999;   99WO-DK00084.
XX
PR   27-FEB-1998;   98DK-0000268.
PR   27-FEB-1998;   98DK-0000272.
XX
PA   (NOVO ) NOVO-NORDISK AS.
XX
PI   Knudsen LB,  Huusfeldt PO,  Nielsen PF,  Kaarsholm NC,  Olsen HB;
PI   Bjorn SE;
XX
DR   WPI; 1999-540500/45.
XX
PT   Composition containing stabilized derivatives of glucagon-like
PT   peptide-1 with high alpha-helix content, for treating diabetes and
PT   obesity
XX
PS   Claim 30; Page -; 63pp; English.
XX
CC   This sequence represents a mutant of the human glucagon-like peptide-1
CC   (GLP-1), and has a helix content (determined by circular dichroism at
CC   222 nm in water at 20-24 degrees C) over 25, preferably 25-50,% at
CC   peptide concentration about 10 microM. The GLP-1 mutant can be used in a
CC   pharmaceutical composition of the invention. The compositions are used to
CC   treat diabetes (both type I and particularly type II) and/or obesity.
CC   They have better solubility and/or stability (against endogenous
CC   diaminopeptidyl peptidase) than parent peptides, with long persistence in
CC   the plasma and retention of biological activity. They form partially
CC   structured micelle-like aggregates in solution, with the helix content
CC   practically independent of concentration.
CC   NOTE: This sequence was created from the human GLP-1 sequence using
CC   information given in the specification.
XX
SQ   Sequence   35 AA;
```

AAY34203 Length: 35 January 22, 2004 18:02 Type: P Check: 7453 ..

1 HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR GRRDF

```
!!AA_SEQUENCE 1.0
ID   AAY28960 standard; Protein; 187 AA.
XX
AC   AAY28960;
XX
DT   04-OCT-1999  (first entry)
XX
DE   Amino acid sequence of a fusion protein G11784HR6GLP-1.
XX
KW   Recombinant peptide production; fusion peptide; accessory peptide;
KW   chemical modification; agglutination.
XX
OS   Synthetic.
XX
PN   WO9938984-A1.
XX
PD   05-AUG-1999.
XX
PF   29-JAN-1999;   99WO-JP00406.
XX
PR   30-JAN-1998;   98JP-0032272.
XX
PA   (SUNR ) SUNTORY LTD.
XX
PI   Ohsuye K,  Suzuki Y,  Yabuta M;
XX
DR   WPI; 1999-469333/39.
XX
```

PT Production of recombinant peptide as a fusion peptide followed by
PT cleavage to give the target peptide in high yield and purity
XX
PS Disclosure; Fig 11; 88pp; Japanese.
XX
CC The invention provides a method for the production of a desired
CC recombinant peptide where the recombinant peptide is produced as a fusion
CC peptide with a suitable accessory peptide. The fusion peptide is purified
CC from culture, subjected to any desired chemical modification, and then
CC cleaved and further purified to yield the desired peptide. The method is
CC used for efficient production of the desired peptides in high yield and
CC purity. The method allows the isoelectric point of the peptide purified
CC from the culture medium to be regulated to prevent agglutination of the
CC peptide and resultant loss of purity. Purity of above 98% and endotoxin
CC content below 0.03 U/mg can be achieved. The present sequence represents
CC the amino acid sequence of a fusion protein G117S4HR6GLP-1 comprising
CC GLP-1, a supplementary peptide and beta-galactosidase protective peptide.
XX
SQ Sequence 187 AA;

AAY28960 Length: 187 January 22, 2004 18:02 Type: P Check: 5975 ..

1 MTMITDSLAV VLQRKDWDNP GVTQLNRLAA HPPFASWRNS DDARTDRPSQ

51 QLRSLNGEWR FAWFPAPEAV PASLLESDLP EADTVVVPSN WQMHGYDAPI

101 YTNVTYPITV NPPFVPTEPH HHHHGGRQMH GYDAELRLYR RHHRWGRSGS

151 PSRHKRHAEG TFTSDVSSYL EGQAAKEFIA WLVKGRG

!!AA_SEQUENCE 1.0
ID AAY28961 standard; Protein; 184 AA.
XX
AC AAY28961;
XX
DT 04-OCT-1999 (first entry)
XX
DE Amino acid sequence of a fusion protein G117S4HompRHKR.
XX
KW Recombinant peptide production; fusion peptide; accessory peptide;
KW chemical modification; agglutination.
XX
OS Synthetic.
XX
PN WO9938984-A1.
XX
PD 05-AUG-1999.
XX
PF 29-JAN-1999; 99WO-JP00406.
XX
PR 30-JAN-1998; 98JP-0032272.
XX
PA (SUNR) SUNTORY LTD.
XX
PI Ohsuye K, Suzuki Y, Yabuta M;
XX
DR WPI; 1999-469333/39.
XX
PT Production of recombinant peptide as a fusion peptide followed by
PT cleavage to give the target peptide in high yield and purity
XX
PS Disclosure; Fig 12; 88pp; Japanese.
XX
CC The invention provides a method for the production of a desired
CC recombinant peptide where the recombinant peptide is produced as a fusion
CC peptide with a suitable accessory peptide. The fusion peptide is purified
CC from culture, subjected to any desired chemical modification, and then
CC cleaved and further purified to yield the desired peptide. The method is
CC used for efficient production of the desired peptides in high yield and
CC purity. The method allows the isoelectric point of the peptide purified
CC from the culture medium to be regulated to prevent agglutination of the
CC peptide and resultant loss of purity. Purity of above 98% and endotoxin
CC content below 0.03 U/mg can be achieved. The present sequence represents
CC the amino acid sequence of a fusion protein G117S4HompRHKR comprising
CC GLP-1, a supplementary peptide and beta-galactosidase protective peptide.
XX
SQ Sequence 184 AA;

AAY28961 Length: 184 January 22, 2004 18:02 Type: P Check: 1204 ..

1 MTMITDSLAV VLQRKDWDNP GVTQLNRLAA HPPFASWRNS DDARTDRPSQ

51 QLRSLNGEWR FAWFPAPEAV PASLLESDLP EADTVVVPSN WQMHGYDAPI

101 YTNVTYPITV NPPFVPTEPH HHHHGGRQMH GYDAELRLYR RHHGSGSPSR

151 HKRHAEGTFT SDVSSYLEGQ AAKEFIAWLV KGRG

!!AA_SEQUENCE 1.0
ID AAY28962 standard; Protein; 184 AA.
XX
AC AAY28962;
XX
DT 04-OCT-1999 (first entry)
XX
DE Amino acid sequence of a fusion protein G117S4HompRHPR.
XX
KW Recombinant peptide production; fusion peptide; accessory peptide;
KW chemical modification; agglutination.
XX
OS Synthetic.
XX
PN WO9938984-A1.
XX
PD 05-AUG-1999.
XX
PF 29-JAN-1999; 99WO-JP00406.
XX
PR 30-JAN-1998; 98JP-0032272.
XX
PA (SUNR) SUNTORY LTD.
XX
PI Ohsuye K, Suzuki Y, Yabuta M;
XX
DR WPI; 1999-469333/39.
XX
PT Production of recombinant peptide as a fusion peptide followed by
PT cleavage to give the target peptide in high yield and purity
XX
PS Disclosure; Fig 13; 88pp; Japanese.
XX
CC The invention provides a method for the production of a desired
CC recombinant peptide where the recombinant peptide is produced as a fusion
CC peptide with a suitable accessory peptide. The fusion peptide is purified
CC from culture, subjected to any desired chemical modification, and then
CC cleaved and further purified to yield the desired peptide. The method is
CC used for efficient production of the desired peptides in high yield and
CC purity. The method allows the isoelectric point of the peptide purified
CC from the culture medium to be regulated to prevent agglutination of the
CC peptide and resultant loss of purity. Purity of above 98% and endotoxin
CC content below 0.03 U/mg can be achieved. The present sequence represents
CC the amino acid sequence of a fusion protein G117S4HompRHPR comprising
CC GLP-1, a supplementary peptide and beta-galactosidase protective peptide.
XX
SQ Sequence 184 AA;

AAY28962 Length: 184 January 22, 2004 18:02 Type: P Check: 1394 ..

1 MTMITDSLAV VLQRKDWDNP GVTQLNRLAA HPPFASWRNS DDARTDRPSQ

51 QLRSLNGEWR FAWFPAPEAV PASLLESDLP EADTVVVPSN WQMHGYDAPI

101 YTNVTYPITV NPPFVPTEPH HHHHGGRQMH GYDAELRLYR RHHGSGSPSR

151 HPRHAEGTFT SDVSSYLEGQ AAKEFIAWLV KGRG

```
!!AA_SEQUENCE 1.0
ID   AAY28959 standard; Protein; 154 AA.
XX
AC   AAY28959;
XX
DT   04-OCT-1999  (first entry)
XX
DE   Amino acid sequence of a fusion protein GP97ompPR.
XX
KW   Recombinant peptide production; fusion peptide; accessory peptide;
KW   chemical modification; agglutination.
XX
OS   Synthetic.
XX
PN   WO9938984-A1.
XX
PD   05-AUG-1999.
XX
PF   29-JAN-1999;   99WO-JP00406.
XX
PR   30-JAN-1998;   98JP-0032272.
XX
PA   (SUNR ) SUNTORY LTD..
XX
PI   Ohsuye K,  Suzuki Y,  Yabuta M;
XX
DR   WPI; 1999-469333/39.
DR   N-PSDB; AAX99247.
XX
PT   Production of recombinant peptide as a fusion peptide followed by
PT   cleavage to give the target peptide in high yield and purity
XX
PS   Disclosure; Fig 7; 88pp; Japanese.
XX
CC   The invention provides a method for the production of a desired
CC   recombinant peptide where the recombinant peptide is produced as a fusion
CC   peptide with a suitable accessory peptide. The fusion peptide is purified
CC   from culture, subjected to any desired chemical modification, and then
CC   cleaved and further purified to yield the desired peptide. The method is
CC   used for efficient production of the desired peptides in high yield and
CC   purity. The method allows the isoelectric point of the peptide purified
CC   from the culture medium to be regulated to prevent agglutination of the
CC   peptide and resultant loss of purity. Purity of above 98% and endotoxin
CC   content below 0.03 U/mg can be achieved. The present sequence represents
CC   the amino acid sequence of a fusion protein GP97ompPR comprising GLP-1, a
CC   supplementary peptide and beta-galactosidase protective peptide.
XX
SQ   Sequence   154 AA;

AAY28959  Length: 154  January 22, 2004 18:02  Type: P  Check: 5814  ..

       1  MTMITDSLAV VLQRKDWDNP GVTQLNRLAA HPPFASWRNS DDARTDRPSQ

      51  QLRSLNGEWR FAWFPAPEAV PASLLESDLP EADTVVVPSN WQMHGYDAMH

     101  GYDAELRLYR RHHGSGSPSR HPRHAEGTFT SDVSSYLEGQ AAKEFIAWLV

     151  KGRG

!!AA_SEQUENCE 1.0
ID   AAY22165 standard; peptide; 31 AA.
XX
AC   AAY22165;
XX
DT   08-SEP-1999  (first entry)
XX
DE   GLP-1-like peptide.
XX
KW   GLP-1-like peptide; glucagon like peptide-1; diabetes; obesity; stroke;
KW   myocardial infarction; catabolic state; therapy.
XX
OS   Synthetic.
XX
PN   WO9929336-A1.
XX
PD   17-JUN-1999.
XX
PF   02-DEC-1998;   98WO-US25515.
XX
PR   05-DEC-1997;   97US-0067600.
XX
PA   (ELIL ) LILLY & CO ELI.
XX
PI   Hoffmann JA;
XX
DR   WPI; 1999-404893/34.
XX
PT   New glucagon-like peptide-1 formulations
XX
PS   Claim 5; Page 22; 26pp; English.
XX
CC   This sequence represets a glucagon-like peptide-1 (GLP-1)-like peptide,
CC   and is used in the formulation of the invention, along with a surfactant.
CC   The formulations can be used for treating conditions for which
CC   administration of GLP-1 is indicated, e.g. diabetes, obesity, myocardial
CC   infarction, catabolic states or stroke. The formulations improve the
CC   storage stability of GLP-1 over a wide range of storage conditions,
CC   e.g. 2-37 degrees C.
XX
SQ   Sequence   31 AA;

 AAY22165  Length: 31  January 22, 2004 18:02  Type: P  Check: 7361  ..

       1  HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID   AAY22167 standard; peptide; 31 AA.
XX
AC   AAY22167;
XX
DT   08-SEP-1999  (first entry)
XX
DE   GLP-1-like peptide.
XX
KW   GLP-1-like peptide; glucagon like peptide-1; diabetes; obesity; stroke;
KW   myocardial infarction; catabolic state; therapy.
XX
OS   Synthetic.
XX
PN   WO9929336-A1.
XX
PD   17-JUN-1999.
XX
PF   02-DEC-1998;   98WO-US25515.
XX
PR   05-DEC-1997;   97US-0067600.
XX
PA   (ELIL ) LILLY & CO ELI.
XX
PI   Hoffmann JA;
XX
DR   WPI; 1999-404893/34.
XX
PT   New glucagon-like peptide-1 formulations
XX
PS   Claim 5; Page 23-24; 26pp; English.
XX
CC   This sequence represets a glucagon-like peptide-1 (GLP-1)-like peptide,
CC   and is used in the formulation of the invention, along with a surfactant.
CC   The formulations can be used for treating conditions for which
CC   administration of GLP-1 is indicated, e.g. diabetes, obesity, myocardial
CC   infarction, catabolic states or stroke. The formulations improve the
CC   storage stability of GLP-1 over a wide range of storage conditions,
CC   e.g. 2-37 degrees C.
XX
SQ   Sequence   31 AA;
```

AAY22167 Length: 31 January 22, 2004 18:02 Type: P Check: 7403 ..

1 HVEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

```
!!AA_SEQUENCE 1.0
ID   AAY18036 standard; peptide; 31 AA.
XX
AC   AAY18036;
XX
DT   03-AUG-1999  (first entry)
XX
DE   GLP-1(7-37)OH peptide.
XX
KW   GLP-1; glucagon-like peptide-1; rod-shaped GLP molecule; diabetes;
KW   plate-like GLP related molecule crystal; crystal preparation; obesity;
KW   therapy.
XX
OS   Homo sapiens.
XX
PN   EP926159-A2.
XX
PD   30-JUN-1999.
XX
PF   14-DEC-1998;   98EP-0310245.
XX
PR   16-DEC-1997;   97US-0069728.
XX
PA   (ELIL ) LILLY & CO ELI.
XX
PI   Hermeling RN,  Hoffmann JA,  Narasimhan C;
XX
DR   WPI; 1999-349221/30.
XX
PT   Preparation of single rod-shaped or plate-like glucagon-like
PT   peptide-1 related molecule crystals, useful for treating diabetes,
PT   obesity etc
XX
PS   Disclosure; Page 3; 17pp; English.
XX
CC   This sequence represents the glucagon-like peptide-1 (GLP-1)
CC   peptide designated GLP-1(7-37)OH.
CC   The invention relates to a method for the preparation of single
CC   rod-shaped or plate-like GLP related molecule crystals comprises,
CC   preparing a crystallization solution comprising a GLP, a buffering agent,
CC   an alcohol or a mono- or disaccharide, and optionally, ammonium sulphate
CC   or zinc. Administration of (a composition comprising) GLP crystals is
CC   useful for treating diabetes, obesity or related conditions. The
CC   tetragonal flat rod shaped or plate-like crystals are less prone to trap
CC   impurities and therefore may be produced in greater yields and
CC   administered more reproducibly. They are also uniform and remain in
CC   suspension for a longer period of time than the crystalline clusters or
CC   amorphous crystalline suspensions which tend to rapidly, aggregate, or
CC   clump together, clog syringe needles and generally exacerbate
CC   unpredictable dosing.
XX
SQ   Sequence   31 AA;
```

AAY18036 Length: 31 January 22, 2004 18:02 Type: P Check: 7361 ..

1 HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

```
!!AA_SEQUENCE 1.0
ID   AAB21328 standard; peptide; 31 AA.
XX
AC   AAB21328;
XX
DT   02-FEB-2001  (first entry)
XX
DE   GLP-1(7-37) peptide.
XX
KW   Glucagon-like peptide-1; GLP-1; peptide acylation;
KW   alkanoyl carboxylate ester.
XX
OS   Unidentified.
XX
PN   WO200055119-A1.
XX
PD   21-SEP-2000.
XX
PF   16-MAR-2000; 2000WO-DK00117.
XX
PR   17-MAR-1999;   99EP-0610019.
XX
PA   (NOVO ) NOVO NORDISK AS.
XX
PI   Hansen LB;
XX
DR   WPI; 2000-628180/60.
XX
PT   Acylating amino group of peptide or protein, for reduoing in vivo
PT   clearance rate, by reacting with alkanoyl carboxylate ester acylating
PT   agent and saponifying acylated peptide ester  -
XX
PS   Claim 11; Page 19; 26pp; English.
XX
CC   The present sequence is part of glucagon-like peptide-1. It was used in a
CC   method for acylating peptides. The method comprises reacting a peptide
CC   with an alkanoyl carboxylate ester acylating agent under basic conditions
CC   in a mixture of an aprotic polar solvent and water, and saponifying the
CC   acylated peptide ester group under basic conditions to obtain an
CC   N-acylated peptide. The method is useful for introducing lipophilic acyl
CC   groups into a peptide or a protein in order to reduce the in vivo
CC   clearance rate of the peptide or protein. The method is especially used
CC   to acylate the epsilon-lysine group in a naturally occurring GLP-1
CC   peptide, such as the present sequence, or GLP-1 analogue.
XX
SQ   Sequence   31 AA;
```

AAB21328 Length: 31 January 22, 2004 18:02 Type: P Check: 7361 ..

1 HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

```
!!AA_SEQUENCE 1.0
ID   AAB21331 standard; peptide; 31 AA.
XX
AC   AAB21331;
XX
DT   02-FEB-2001  (first entry)
XX
DE   GLP-1 analogue Val8GLP-1(7-37).
XX
KW   Glucagon-like peptide-1; GLP-1; peptide acylation;
KW   alkanoyl carboxylate ester; mutant.
XX
OS   Synthetic.
XX
PN   WO200055119-A1.
XX
PD   21-SEP-2000.
XX
PF   16-MAR-2000; 2000WO-DK00117.
XX
PR   17-MAR-1999;   99EP-0610019.
XX
PA   (NOVO ) NOVO NORDISK AS.
XX
PI   Hansen LB;
XX
DR   WPI; 2000-628180/60.
XX
PT   Acylating amino group of peptide or protein, for reducing in vivo
PT   clearance rate, by reacting with alkanoyl carboxylate ester acylating
PT   agent and saponifying acylated peptide ester  -
XX
PS   Claim 12; Page 19; 26pp; English.
```

```
XX
CC   The present sequence is an analogue of part of glucagon-like peptide-1.
CC   It was used in a method for acylating peptides. The method comprises
CC   reacting a peptide with an alkanoyl carboxylate ester acylating agent
CC   under basic conditions in a mixture of an aprotic polar solvent and
CC   water, and saponifying the acylated peptide ester group under basic
CC   conditions to obtain an N-acylated peptide. The method is useful for
CC   introducing lipophilic acyl groups into a peptide or a protein in order
CC   to reduce the in vivo clearance rate of the peptide or protein. The
CC   method is especially used to acylate the epsilon-lysine group in a
CC   naturally occurring GLP-1 peptide or an analogue, such as the present
CC   sequence.
XX
SQ   Sequence   31 AA;

 AAB21331  Length: 31  January 22, 2004 18:02  Type: P  Check: 7403  ..

       1  HVEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID   AAB21334 standard; peptide; 31 AA.
XX
AC   AAB21334;
XX
DT   02-FEB-2001  (first entry)
XX
DE   GLP-1 analogue Gly8-GLP-1(7-37).
XX
KW   Glucagon-like peptide-1; GLP-1; peptide acylation;
KW   alkanoyl carboxylate ester; mutant.
XX
OS   Synthetic.
XX
PN   WO200055119-A1.
XX
PD   21-SEP-2000.
XX
PF   16-MAR-2000; 2000WO-DK00117.
XX
PR   17-MAR-1999;   99EP-0610019.
XX
PA   (NOVO ) NOVO NORDISK AS.
XX
PI   Hansen LB;
XX
DR   WPI; 2000-628180/60.
XX
PT   Acylating amino group of peptide or protein, for reducing in vivo
PT   clearance rate, by reacting with alkanoyl carboxylate ester acylating
PT   agent and saponifying acylated peptide ester  -
XX
PS   Claim 12; Page 19; 26pp; English.
XX
CC   The present sequence is an analogue of part of glucagon-like peptide-1.
CC   It was used in a method for acylating peptides. The method comprises
CC   reacting a peptide with an alkanoyl carboxylate ester acylating agent
CC   under basic conditions in a mixture of an aprotic polar solvent and
CC   water, and saponifying the acylated peptide ester group under basic
CC   conditions to obtain an N-acylated peptide. The method is useful for
CC   introducing lipophilic acyl groups into a peptide or a protein in order
CC   to reduce the in vivo clearance rate of the peptide or protein. The
CC   method is especially used to acylate the epsilon-lysine group in a
CC   naturally occurring GLP-1 peptide or an analogue, such as the present
CC   sequence.
XX
SQ   Sequence   31 AA;

 AAB21334  Length: 31  January 22, 2004 18:02  Type: P  Check: 7373  ..

       1  HGEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID   AAB21339 standard; peptide; 31 AA.
XX
AC   AAB21339;
XX
DT   02-FEB-2001  (first entry)
XX
DE   GLP-1(7-37) peptide.
XX
KW   GLP-1; glucagon-like peptide-1; ion exchange chromatography;
KW   GLP-1 purification; organic modifier.
XX
OS   Unidentified.
XX
PN   WO200055203-A1.
XX
PD   21-SEP-2000.
XX
PF   15-MAR-2000; 2000WO-DK00113.
XX
PR   15-MAR-1999;   99DK-0000361.
PR   19-JAN-2000; 2000DK-0000082.
XX
PA   (NOVO ) NOVO NORDISK AS.
XX
PI   Staby A;
XX
DR   WPI; 2000-618898/59.
XX
PT   Ion exchange chromatographic separation process for separating glucagon
PT   like peptide-1, its analog or derivative from a mixture containing the
PT   peptide and other related impurities, comprises use of a organic
PT   modifier for elution  -
XX
PS   Claim 9; Page 55; 76pp; English.
XX
CC   The present sequence is a portion of glucagon-like peptide-1 (GLP-1). An
CC   ion exchange chromatography process has been developed for purifying
CC   GLP-1, its analogue or derivative, from a mixture comprising GLP-1 and
CC   impurities. The process uses an organic modifier in the elution step. The
CC   pH of the aqueous elution medium supports a net charge distribution on
CC   the protein or peptide that differs from the net charge of the
CC   impurities. The addition of an organic modifier in the elution step
CC   results in an increase in selectivity and efficiency compared to
CC   the same run with aqueous buffers, both for anion and cation exchange
CC   chromatography. The use of an organic modifier has the additional
CC   advantage that no salt, or a very low concentration of salt, is needed
CC   for elution. The naturally occurring GLP-1 and its analogues may be
CC   produced by integrating the DNA coding sequence into an expression
CC   vector. A secretory signal sequence may be provided in the vector in
CC   order to produce a fusion peptide which is directed into the secretory
CC   pathway of host cells.
XX
SQ   Sequence   31 AA;

 AAB21339  Length: 31  January 22, 2004 18:02  Type: P  Check: 7361  ..

       1  HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID   AAB21347 standard; peptide; 31 AA.
XX
AC   AAB21347;
XX
DT   02-FEB-2001  (first entry)
XX
DE   GLP-1 analogue #7.
XX
KW   GLP-1; glucagon-like peptide-1; ion exchange chromatography;
KW   GLP-1 purification; organic modifier; mutant.
XX
OS   Synthetic.
XX
PN   WO200055203-A1.
XX
```

PD 21-SEP-2000.
XX
PF 15-MAR-2000; 2000WO-DK00113.
XX
PR 15-MAR-1999; 99DK-0000361.
PR 19-JAN-2000; 2000DK-0000082.
XX
PA (NOVO) NOVO NORDISK AS.
XX
PI Staby A;
XX
DR WPI; 2000-618898/59.
XX
PT Ion exchange chromatographic separation process for separating glucagon
PT like peptide-1, its analog or derivative from a mixture containing the
PT peptide and other related impurities, comprises use of a organic
PT modifier for elution -
XX
PS Claim 9; Page 55; 76pp; English.
XX
CC The present sequence is glucagon-like peptide-1 (GLP-1) analogue
CC Val8GLP-1(7-37). An ion exchange chromatography process has been
CC developed for purifying GLP-1, its analogues or derivatives, from a
CC mixture comprising GLP-1 and impurities. The process uses an organic
CC modifier in the elution step. The pH of the aqueous elution medium
CC supports a net charge distribution on the protein or peptide that
CC differs from the net charge of the impurities. The addition of an
CC organic modifier in the elution step results in an increase in
CC selectivity and efficiency compared to the same run with aqueous
CC buffers, both for anion and cation exchange chromatography. The use
CC of an organic modifier has the additional advantage that no salt,
CC or a very low concentration of salt, is needed for elution. The
CC naturally occurring GLP-1 and its analogues may be produced by
CC integrating the DNA coding sequence into an expression vector. A
CC secretory signal sequence may be provided in the vector in order
CC to produce a fusion peptide which is directed into the secretory
CC pathway of host cells.
XX
SQ Sequence 31 AA;

AAB21347 Length: 31 January 22, 2004 18:02 Type: P Check: 7403 ..

1 HVEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID AAB21350 standard; peptide; 31 AA.
XX
AC AAB21350;
XX
DT 02-FEB-2001 (first entry)
XX
DE GLP-1 analogue #10.
XX
KW GLP-1; glucagon-like peptide-1; ion exchange chromatography;
KW GLP-1 purification; organic modifier; mutant.
XX
OS Synthetic.
XX
PN WO200055203-A1.
XX
PD 21-SEP-2000.
XX
PF 15-MAR-2000; 2000WO-DK00113.
XX
PR 15-MAR-1999; 99DK-0000361.
PR 19-JAN-2000; 2000DK-0000082.
XX
PA (NOVO) NOVO NORDISK AS.
XX
PI Staby A;
XX
DR WPI; 2000-618898/59.
XX
PT Ion exchange chromatographic separation process for separating glucagon
PT like peptide-1, its analog or derivative from a mixture containing the
PT peptide and other related impurities, comprises use of a organic
PT modifier for elution -
XX
PS Claim 9; Page 56; 76pp; English.
XX
CC The present sequence is glucagon-like peptide-1 (GLP-1) analogue
CC Gly8GLP-1(7-37). An ion exchange chromatography process has been
CC developed for purifying GLP-1, its analogues or derivatives, from a
CC mixture comprising GLP-1 and impurities. The process uses an organic
CC modifier in the elution step. The pH of the aqueous elution medium
CC supports a net charge distribution on the protein or peptide that
CC differs from the net charge of the impurities. The addition of an
CC organic modifier in the elution step results in an increase in
CC selectivity and efficiency compared to the same run with aqueous
CC buffers, both for anion and cation exchange chromatography. The use
CC of an organic modifier has the additional advantage that no salt,
CC or a very low concentration of salt, is needed for elution. The
CC naturally occurring GLP-1 and its analogues may be produced by
CC integrating the DNA coding sequence into an expression vector. A
CC secretory signal sequence may be provided in the vector in order
CC to produce a fusion peptide which is directed into the secretory
CC pathway of host cells.
XX
SQ Sequence 31 AA;

AAB21350 Length: 31 January 22, 2004 18:02 Type: P Check: 7373 ..

1 HGEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID AAB21109 standard; protein; 31 AA.
XX
AC AAB21109;
XX
DT 19-JAN-2001 (first entry)
XX
DE Human glucagon-like peptide-1 GLP-1(7-37).
XX
KW Human; glucagon like peptide-1; GLP-1(7-37); agonist;
KW impaired glucose tolerance; diabetes; obesity.
XX
OS Homo sapiens.
XX
PN WO200042026-A1.
XX
PD 20-JUL-2000.
XX
PF 14-JAN-2000; 2000WO-DK00014.
XX
PR 15-JAN-1999; 99DK-0000041.
XX
PA (NOVO) NOVO NORDISK AS.
PA (AGOU-) AGOURON PHARM INC.
XX
PI Teng M, Truesdale LK, Bhumralkar D, Kiel D, Johnson MD, Thomas C;
PI Jorgensen AS, Madsen P, Olesen PH, Knudsen LB, Petterson IV;
PI Cornelis De Jong J, Behrens C, Kodra JT, Lau J;
XX
DR WPI; 2000-499091/44.
XX
PT New quinoline and quinoxaline derivatives are non-peptide glucagon like
PT peptide-1 agonists used for treating e.g. impaired glucose tolerance
PT and type 2 diabetes -
XX
PS Disclosure; Page 1; 194pp; English.
XX
CC The present sequence is the (7-37) form of the human glucagon like
CC peptide-1 (GLP-1). GLP-1 is an incretin and functions to stimulate
CC insulin secretion, decrease glucagon secretion, inhibit gastric emptying,
CC decrease appetite and stimulate proliferation of beta-cells. The
CC invention provides a number of GLP-1 agonists which can be used to treat

CC metabolic disorders, hyperglycaemia, dyslipidaemia, diabetes (Type 1 and
CC 2), hypertriglyceridaemia, syndrome X, insulin resistance, impaired
CC glucose tolerance, obesity, hyperlipidaemia, cardiovascular diseases,
CC eating disorders, anxiety, movement disorder, aggression, psychosis,
CC seizures, panic attacks, hysteria, sleep disorders and hypertension.
XX
SQ Sequence 31 AA;

AAB21109 Length: 31 January 22, 2004 18:02 Type: P Check: 7361 ..

1 HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID AAB23948 standard; Protein; 184 AA.
XX
AC AAB23948;
XX
DT 19-JAN-2001 (first entry)
XX
DE Plasmid pG117S4H ompRHPR protein sequence SEQ ID NO:5.
XX
KW OmpT protease; cleavage; fusion protein; membrane protease;
KW natriuretic; Escherichia coli.
XX
OS Escherichia coli.
OS Synthetic.
XX
PN WO200052193-A1.
XX
PD 08-SEP-2000.
XX
PF 03-MAR-2000; 2000WO-JP01309.
XX
PR 04-MAR-1999; 99JP-0057731.
XX
PA (SUNR) SUNTORY LTD.
XX
PI Okuno K, Yabuta M, Ohsuye K;
XX
DR WPI; 2000-579291/54.
XX
PT Controlled cleavage of peptides by OmpT protease by amino acid
PT substitution for ensuring cleavage only at desired site in fission of
PT fusion proteins -
XX
PS Example 1; Fig 4; 144pp; Japanese.
XX
CC The present invention describes a method for regulating the cleavage
CC sites of polypeptides by OmpT protease by preventing cleavage at
CC unwanted sites by converting the amino acid residue at position +1 to
CC the site to a specifically defined amino acid (where the residue at
CC position -1 to the site is Lys or Arg), and/or converting the residue
CC at position -4 and/or -6 to a specifically defined amino acid. Also
CC described is a method for the fission of a fusion protein to give a
CC desired polypeptide by cleavage with OmpT protease, where the fusion
CC protein has a linker peptide inserted between the desired polypeptide
CC and the other part of the fusion protein. The fusion protein may be
CC prepared by expression of DNA encoding in a suitable host cell such as
CC Escherichia coli. OmpT protease is a membrane protease of Escherichia
CC coli which cleaves peptide chains at a two-residue sites in which both
CC residues are basic amino acids such as arginine or lysine. The methods
CC can be used for the efficient preparation of undegraded desired
CC polypeptides such as natriuretic peptide by OmpT protease cleavage after
CC recombinant expression as a fusion protein. AAA99127 to AAA99177 and
CC AAB23946 to AAB24018 represent sequences used in the exemplification of
CC the present invention.
XX
SQ Sequence 184 AA;

AAB23948 Length: 184 January 22, 2004 18:02 Type: P Check: 1498 ..

1 MTMITDSLAV VLQRKDWENP GVTQLNRLAA HPPFASWRNS DDARTDRPSQ

51 QLRSLNGEWR FAWFPAPEAV PESLLDLPEA DTVVVPDSSN WQMHGYDAPI

101 YTNVTYPITV NPPFVPTEPH HHHPGGRQMH GYDAELRLYR RHEGSGSPSR

151 HPRHAEGTFT SDVSSYLEGQ AAKEFIAWLV KGRG

!!AA_SEQUENCE 1.0
ID AAB26773 standard; Protein; 180 AA.
XX
AC AAB26773;
XX
DT 17-JAN-2001 (first entry)
XX
DE Rat preproglucagon amino acid sequence.
XX
KW Amylin; production; secretory cell; blood glucose level regulation;
KW diabetes mellitus; hypoglycaemia; osteoporosis; Paget's disease;
KW hypercalcaemia; obesity; hypertension.
XX
OS Rattus sp.
XX
PN US6110707-A.
XX
PD 29-AUG-2000.
XX
PF 17-JAN-1997; 97US-0784582.
XX
PR 11-OCT-1996; 96US-0028279.
PR 19-JAN-1996; 96US-0589028.
XX
PA (TEXA) UNIV TEXAS SYSTEM.
PA (BETA-) BETAGENE INC.
XX
PI Newgard CB, Halban P, Normington KD, Thigpen AE, Quaade C;
PI Kruse F, McGarry D, Clark SA;
XX
DR WPI; 2000-586352/55.
DR N-PSDB; AAC55762.
XX
PT Producing mammalian amylin, useful for regulating blood glucose and
PT insulin levels, e.g. for treating diabetes mellitus or hypoglycemia, by
PT employing recombinantly engineered secretory cell lines -
XX
PS Example 10; Column 175-176; 136pp; English.
XX
CC This invention relates to a method for producing mammalian amylin. The
CC method relies on the use of a recombinantly engineered secretory cell
CC line. The method comprises:
CC (a) providing a starting secretory cell that has a regulated secretory
CC pathway;
CC (b) introducing, into the starting secretory cell, an amylin-encoding
CC gene operatively linked to a first promoter;
CC (c) selecting a secretory cell of (b) that exhibits increased production
CC of biologically active amylin as compared to the starting secretory
CC cell; and (d) culturing the selected secretory cell.
CC Amylin is an insulin modulator, and the method results in antidiabetic,
CC hypotensive and osteopathic activity. The amylins produced are useful
CC for regulating blood glucose levels, as well as in modulating the
CC circulating levels of insulin in a mammal. The amylins produced maybe
CC used in treating diabetes mellitus, hypoglycaemia, osteoporosis, Paget's
CC disease, hypercalcaemia, obesity, hypertension, or any other disorder
CC requiring amylin regulation. The invention includes cDNA and protein
CC sequences (AAC55760 and AAB26771) representing human amylin. Sequences
CC AAC55716-C55681 and AAB26765-B26777 are used in examples of the method of
CC the invention for the production of mammalian amylin.
XX
SQ Sequence 180 AA;

AAB26773 Length: 180 January 22, 2004 18:02 Type: P Check: 8911 ..

1 MKTVYIVAGL FVMLVQGSWQ HAPQDTEENA RSFPASQTEP LEDPDQINED

51 KRHSQGTFTS DYSKYLDSRR AQDFVQWLMN TKRNRNNIAK RHDEFERHAE

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     101  GTFTSDVSSY LEGQAAKEFI AWLVKGRGER DFPEEVAIAE ELGRRHADGS

     151  FSDEMNTILD NLATRDFINW LIQTKITDKK

!!AA_SEQUENCE 1.0
ID   AAB26774 standard; Protein; 180 AA.
XX
AC   AAB26774;
XX
DT   17-JAN-2001  (first entry)
XX
DE   Human preproglucagon amino acid sequence.
XX
KW   Amylin; production; secretory cell; blood glucose level regulation;
KW   diabetes mellitus; hypoglycaemia; osteoporosis; Paget's disease;
KW   hypercalcaemia; obesity; hypertension.
XX
OS   Homo sapiens.
XX
PN   US6110707-A.
XX
PD   29-AUG-2000.
XX
PF   17-JAN-1997;   97US-0784582.
XX
PR   11-OCT-1996;   96US-0028279.
PR   19-JAN-1996;   96US-0589028.
XX
PA   (TEXA ) UNIV TEXAS SYSTEM.
PA   (BETA-) BETAGENE INC.
XX
PI   Newgard CB,  Halban P,  Normington KD,  Thigpen AE,  Quaade C;
PI   Kruse F,  McGarry D,  Clark SA;
XX
DR   WPI; 2000-586352/55.
DR   N-PSDB; AAC55763.
XX
PT   Producing mammalian amylin, useful for regulating blood glucose and
PT   insulin levels, e.g. for treating diabetes mellitus or hypoglycemia, by
PT   employing recombinantly engineered secretory cell lines -
XX
PS   Example 10; Column 177-178; 136pp; English.
XX
CC   This invention relates to a method for producing mammalian amylin. The
CC   method relies on the use of a recombinantly engineered secretory cell
CC   line. The method comprises:
CC   (a) providing a starting secretory cell that has a regulated secretory
CC   pathway;
CC   (b) introducing, into the starting secretory cell, an amylin-encoding
CC   gene operatively linked to a first promoter;
CC   (c) selecting a secretory cell of (b) that exhibits increased production
CC   of biologically active amylin as compared to the starting secretory
CC   cell; and (d) culturing the selected secretory cell.
CC   Amylin is an insulin modulator, and the method results in antidiabetic,
CC   hypotensive and osteopathic activity. The amylins produced are useful
CC   for regulating blood glucose levels, as well as in modulating the
CC   circulating levels of insulin in a mammal. The amylins produced maybe
CC   used in treating diabetes mellitus, hypoglycaemia, osteoporosis, Paget's
CC   disease, hypercalcaemia, obesity, hypertension, or any other disorder
CC   requiring amylin regulation. The invention includes cDNA and protein
CC   sequences (AAC55760 and AAB26771) representing human amylin. Sequences
CC   AAC55716-C55681 and AAB26765-B26777 are used in examples of the method of
CC   the invention for the production of mammalian amylin.
XX
SQ   Sequence   180 AA;

AAB26774  Length: 180  January 22, 2004 18:02  Type: P  Check: 9748  ..

       1  MKSIYFVAGL FVMLVQGSWQ RSLQDTEEKS RSFSASQADP LSDPDQMNED

      51  KRHSQGTFTS DYSKYLDSRR AQDFVQWLMN TKRNRNNIAK RHDEFERHAE
```

```
     101  GTFTSDVSSY LEGQAAKEFI AWLVKGRGRR DFPEEVAIVE ELGRRHADGS

     151  FSDEMNTILD NLAARDFINW LIQTKITDRK

!!AA_SEQUENCE 1.0
ID   AAB26775 standard; Protein; 180 AA.
XX
AC   AAB26775;
XX
DT   17-JAN-2001  (first entry)
XX
DE   Mutant human preproglucagon amino acid sequence.
XX
KW   Amylin; production; secretory cell; blood glucose level regulation;
KW   diabetes mellitus; hypoglycaemia; osteoporosis; Paget's disease;
KW   hypercalcaemia; obesity; hypertension.
XX
OS   Homo sapiens.
XX
PN   US6110707-A.
XX
PD   29-AUG-2000.
XX
PF   17-JAN-1997;   97US-0784582.
XX
PR   11-OCT-1996;   96US-0028279.
PR   19-JAN-1996;   96US-0589028.
XX
PA   (TEXA ) UNIV TEXAS SYSTEM.
PA   (BETA-) BETAGENE INC.
XX
PI   Newgard CB,  Halban P,  Normington KD,  Thigpen AE,  Quaade C;
PI   Kruse F,  McGarry D,  Clark SA;
XX
DR   WPI; 2000-586352/55.
DR   N-PSDB; AAC55765.
XX
PT   Producing mammalian amylin, useful for regulating blood glucose and
PT   insulin levels, e.g. for treating diabetes mellitus or hypoglycemia, by
PT   employing recombinantly engineered secretory cell lines -
XX
PS   Example 10; Column 179-182; 136pp; English.
XX
CC   This invention relates to a method for producing mammalian amylin. The
CC   method relies on the use of a recombinantly engineered secretory cell
CC   line. The method comprises:
CC   (a) providing a starting secretory cell that has a regulated secretory
CC   pathway;
CC   (b) introducing, into the starting secretory cell, an amylin-encoding
CC   gene operatively linked to a first promoter;
CC   (c) selecting a secretory cell of (b) that exhibits increased production
CC   of biologically active amylin as compared to the starting secretory
CC   cell; and (d) culturing the selected secretory cell.
CC   Amylin is an insulin modulator, and the method results in antidiabetic,
CC   hypotensive and osteopathic activity. The amylins produced are useful
CC   for regulating blood glucose levels, as well as in modulating the
CC   circulating levels of insulin in a mammal. The amylins produced maybe
CC   used in treating diabetes mellitus, hypoglycaemia, osteoporosis, Paget's
CC   disease, hypercalcaemia, obesity, hypertension, or any other disorder
CC   requiring amylin regulation. The invention includes cDNA and protein
CC   sequences (AAC55760 and AAB26771) representing human amylin. Sequences
CC   AAC55716-C55681 and AAB26765-B26777 are used in examples of the method of
CC   the invention for the production of mammalian amylin.
XX
SQ   Sequence   180 AA;

AAB26775  Length: 180  January 22, 2004 18:02  Type: P  Check: 8864  ..

       1  MKSIYFVAGL FVMLVQGSWQ RSLQDTEEKS RSFSASQADP LSDPDQMNED

      51  KAHSQGTFTS DYSKYLDSRR AQDFVQWLMN TKRNRNNIAK RHDEFERHAE

     101  GTFTSDVSSY LEGQAAKEFI AWLVKGRGRR DFPEEVAIVE ELGRRHADGS
```

```
     151  FSDEMNTILD NLAARDFINW LIQTKITDRK

!!AA_SEQUENCE 1.0
ID   AAB26777 standard; Protein; 360 AA.
XX
AC   AAB26777;
XX
DT   17-JAN-2001  (first entry)
XX
DE   Human growth hormone and mutated proglucagon fusion protein.
XX
KW   Amylin; production; secretory cell; blood glucose level regulation;
KW   diabetes mellitus; hypoglycaemia; osteoporosis; Paget's disease;
KW   hypercalcaemia; obesity; hypertension.
XX
OS   Homo sapiens.
XX
PN   US6110707-A.
XX
PD   29-AUG-2000.
XX
PF   17-JAN-1997;   97US-0784582.
XX
PR   11-OCT-1996;   96US-0028279.
PR   19-JAN-1996;   96US-0589028.
XX
PA   (TEXA ) UNIV TEXAS SYSTEM.
PA   (BETA-) BETAGENE INC.
XX
PI   Newgard CB,  Halban P,  Normington KD,  Thigpen AE,  Quaade C;
PI   Kruse F,  McGarry D,  Clark SA;
XX
DR   WPI; 2000-586352/55.
DR   N-PSDB; AAC55775.
XX
PT   Producing mammalian amylin, useful for regulating blood glucose and
PT   insulin levels, e.g. for treating diabetes mellitus or hypoglycemia, by
PT   employing recombinantly engineered secretory cell lines -
XX
PS   Example 12; Column 189-192; 136pp; English.
XX
CC   This invention relates to a method for producing mammalian amylin. The
CC   method relies on the use of a recombinantly engineered secretory cell
CC   line. The method comprises:
CC   (a) providing a starting secretory cell that has a regulated secretory
CC   pathway;
CC   (b) introducing, into the starting secretory cell, an amylin-encoding
CC   gene operatively linked to a first promoter;
CC   (c) selecting a secretory cell of (b) that exhibits increased production
CC   of biologically active amylin as compared to the starting secretory
CC   cell; and (d) culturing the selected secretory cell.
CC   Amylin is an insulin modulator, and the method results in antidiabetic,
CC   hypotensive and osteopathic activity. The amylins produced are useful
CC   for regulating blood glucose levels, as well as in modulating the
CC   circulating levels of insulin in a mammal. The amylins produced maybe
CC   used in treating diabetes mellitus, hypoglycaemia, osteoporosis, Paget's
CC   disease, hypercalcaemia, obesity, hypertension, or any other disorder
CC   requiring amylin regulation. The invention includes cDNA and protein
CC   sequences (AAC55760 and AAB26771) representing human amylin. Sequences
CC   AAC55716-C55681 and AAB26765-B26777 are used in examples of the method of
CC   the invention for the production of mammalian amylin.
XX
SQ   Sequence   360 AA;

AAB26777  Length: 360  January 22, 2004 18:02  Type: P  Check: 8646  ..

       1  MATGSRTSLL LAFGLLCLPW LQEGSAFPTI PLSRLFDNAM LRAHRLHQLA

      51  FDTYQEFEEA YIPKEQKYSF LQNPQTSLCF SESIPTPSNR EETQQKSNLE

     101  LLRISLLLIQ SWLEPVQFLR SVFANSLVYG ASDSNVYDLL KDLEEGIQTL

     151  MGRLEDGSPR TGQIFKQTYS KFDTNSHNDD ALLKNYGLLY CFRKDMDKVQ

     201  RSLQDTEEKS RSFSASQADP LSDPDQMNED KAHSQGTFTS DYSKYLDSRR

     251  AQDFVQWLMN TKRNRNNIAK RHDEFERHAE GTFTSDVSSY LEGQAAKEFI

     301  AWLVKGRGRR DFPEEVAIVE ELGRRHADGS FSDEMNTILD NLAARDFINW

     351  LIQTKITDRK

!!AA_SEQUENCE 1.0
ID   AAB11889 standard; peptide; 31 AA.
XX
AC   AAB11889;
XX
DT   14-NOV-2000  (first entry)
XX
DE   Shelf-stable glucagon-like peptide-1 (GLP-1) analogue.
XX
KW   Glucagon-like peptide-1; GLP-1 analogue; insulin secretion regulator;
KW   insulin expression enhancer; shelf stable formulation;
KW   drug delivery; continuous infusion system; pen delivery device;
KW   type II diabetes; non insulin dependent diabetes.
XX
OS   Synthetic.
OS   Mammalia.
XX
PN   WO200037098-A1.
XX
PD   29-JUN-2000.
XX
PF   21-DEC-1999;   99WO-US30395.
XX
PR   22-DEC-1998;   98US-0113499.
XX
PA   (ELIL ) LILLY & CO ELI.
XX
PI   Brader ML,  Pekar AH;
XX
DR   WPI; 2000-442534/38.
XX
PT   Shelf-stable pharmaceutical formulation useful for treating diabetes
PT   comprises glucagon-like peptide-1 molecule, preservative and tonicity
PT   modifier  -
XX
PS   Claim 7; Page -; 27pp; English.
XX
CC   The invention relates to a shelf-stable glucagon-like peptide-1 (GLP-1)
CC   formulation comprising a GLP-1 molecule, a preservative and a tonicity
CC   modifier and has a pH of 8.2-8.8. GLP-1 regulates insulin secretion in
CC   response to glucose, enhancing the expression of insulin in a mammalian
CC   pancreatic beta-type islet cell, and thus has the ability to normalise
CC   blood glucose levels. There has therefore been considerable interest in
CC   the use of GLP-1 for the treatment of type II (non insulin dependent)
CC   diabetes, and it has been shown that doses in the 1-5 nanomole range
CC   exhibit few side effects, and that GLP-1 is effective in patients that
CC   have secondary failure to sulphonylurea drugs. However, GLP-1 peptides
CC   have poor long term stability, a fairly short biological half-life and
CC   are highly soluble in aqueous solutions such as neutral phosphate
CC   buffered saline, which limits their use in continuous infusion systems
CC   and pen delivery devices. The formulation of the invention has increased
CC   physical and chemical stability relative to conventional peptide
CC   formulations, which enables it to be used in such delivery devices. One
CC   embodiment of the invention also comprises a long-acting diabetic agent,
CC   thus providing meal-time glycaemic control and basal glycaemic control
CC   with a single injection. The present sequence represents a specific
CC   GLP-1 analogue which may be used in the formulation of the invention.
CC   Note: The present sequence is not shown in the specification, but is
CC   derived from the generic SEQ ID NO:2 (AAB11888) and the information
CC   provided on page 17 (claim 7).
XX
SQ   Sequence   31 AA;
```

```
AAB11889  Length: 31  January 22, 2004 18:02  Type: P  Check: 7403  ..

      1  HVEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID   AAY96846 standard; Protein; 127 AA.
XX
AC   AAY96846;
XX
DT   26-SEP-2000  (first entry)
XX
DE   PCpB-QAR-V8-GLIP fusion protein.
XX
KW   PCpB; propeptide; procaboxypeptidase B; fusion protein; beta-lipotropin;
KW   BLT; hPTH (1-34); human parathyroid hormone; V8-GLIP; analgesic;
KW   glucagon-like insulinotropic peptide; heterologous protein production;
KW   melanin synthesis; glucocorticoid release; trypsin.
XX
OS   Chimeric - Sus scrofa.
OS   Chimeric - Homo sapiens.
OS   Chimeric - Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1. .93
FT                   /label= Porcine_Procarboxypeptidase-B_propeptide
FT   Cleavage-site   94. .96
FT                   /note= "trypsin cleavage site"
FT   Protein         97. .127
FT                   /label= Human_glucagon-like_insulinotropic_peptide
XX
PN   WO200037615-A1.
XX
PD   29-JUN-2000.
XX
PF   15-DEC-1999;   99WO-US29837.
XX
PR   21-DEC-1998;   98US-0113058.
XX
PA   (ELIL ) LILLY & CO ELI.
XX
PI   Hale JE,  Hershberger CL,  Larson JL,  Menke MA;
XX
DR   WPI; 2000-442656/38.
DR   N-PSDB; AAA51465.
XX
PT   Novel methods and nucleic acids for producing fusion proteins
PT   comprising a procaboxypeptidase B propeptide sequence
XX
PS   Disclosure; Page 102; 120pp; English.
XX
CC   Novel fusion proteins comprise a propeptide sequence of (porcine)
CC   procaboxypeptidase B (PCpB). The fusion proteins can be used for
CC   producing, e.g. human beta-lipotropin (BLT) and other peptides in
CC   Escherichia coli and yeast. The PCpB sequence provides solubility to the
CC   fusion proteins, induces a high level of fusion protein expression, and
CC   enhances the heat stability of the fusion protein. This is advantageous
CC   because BLT and other small peptides are difficult to purify from whole
CC   tissues. BLT is derived from pro-opiomelanocortin (POMC) a neuropeptide
CC   cleaved by specific endopeptidases. POMC also yields beta-endorphin,
CC   adrenocorticotrophic hormone and melanocyte stimulating hormone.
CC   POMC-derived peptides have important roles in metabolic and physiological
CC   regulation, including secretion of glucocorticoids, stimulating melanin
CC   synthesis, fat metabolism and analgesic activity. The fusion proteins may
CC   by produced in a fungal fusion system that additionally comprise fusion
CC   partners, such as the alpha-mating factor (AMF), propeptide, human serum
CC   albumin (HSA) and any other sequence that promotes expression and
CC   secretion of the fusion protein, and subsequent cleavage (during
CC   secretion from the fungal cell) to release heterologous protein into the
CC   culture medium. The heterologous protein is especially BLT, human
CC   parathyroid hormone (hPTH) (residues 1-34) and V8-GLIP
CC   (glucagon-like insulinotropic peptide) (claimed).
XX
SQ   Sequence   127 AA;
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AAY96846  Length: 127  January 22, 2004 18:02  Type: P  Check: 1278  ..

      1  MHHSGEHFEG EKVFRVNVED ENDISLLHEL ASTRQIDFWK PDSVTQIKPH

     51  STVDFRVKAE DILAVEDFLE QNELQYEVLI NNLRSVLEAQ FDSQARHVEG

    101  TFTSDVSSYL EGQAAKEFIA WLVKGRG

!!AA_SEQUENCE 1.0
ID   AAY96847 standard; Protein; 128 AA.
XX
AC   AAY96847;
XX
DT   26-SEP-2000  (first entry)
XX
DE   PCpB-LVPR-V8-GLIP fusion protein.
XX
KW   PCpB; propeptide; procaboxypeptidase B; fusion protein; beta-lipotropin;
KW   BLT; hPTH (1-34); human parathyroid hormone; V8-GLIP; analgesic;
KW   glucagon-like insulinotropic peptide; heterologous protein production;
KW   melanin synthesis; glucocorticoid release; trypsin; thrombin.
XX
OS   Chimeric - Sus scrofa.
OS   Chimeric - Homo sapiens.
OS   Chimeric - Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1. .93
FT                   /label= Porcine_Procarboxypeptidase-B_propeptide
FT   Cleavage-site   94. .97
FT                   /note= "trypsin cleavage site"
FT   Protein         98. .128
FT                   /label= Human_glucagon-like_insulinotropic_peptide
XX
PN   WO200037615-A1.
XX
PD   29-JUN-2000.
XX
PF   15-DEC-1999;   99WO-US29837.
XX
PR   21-DEC-1998;   98US-0113058.
XX
PA   (ELIL ) LILLY & CO ELI.
XX
PI   Hale JE,  Hershberger CL,  Larson JL,  Menke MA;
XX
DR   WPI; 2000-442656/38.
DR   N-PSDB; AAA51466.
XX
PT   Novel methods and nucleic acids for producing fusion proteins
PT   comprising a procaboxypeptidase B propeptide sequence
XX
PS   Disclosure; Page 103-104; 120pp; English.
XX
CC   Novel fusion proteins comprise a propeptide sequence of (porcine)
CC   procaboxypeptidase B (PCpB). The fusion proteins can be used for
CC   producing, e.g. human beta-lipotropin (BLT) and other peptides in
CC   Escherichia coli and yeast. The PCpB sequence provides solubility to the
CC   fusion proteins, induces a high level of fusion protein expression, and
CC   enhances the heat stability of the fusion protein. This is advantageous
CC   because BLT and other small peptides are difficult to purify from whole
CC   tissues. BLT is derived from pro-opiomelanocortin (POMC) a neuropeptide
CC   cleaved by specific endopeptidases. POMC also yields beta-endorphin,
CC   adrenocorticotrophic hormone and melanocyte stimulating hormone.
CC   POMC-derived peptides have important roles in metabolic and physiological
CC   regulation, including secretion of glucocorticoids, stimulating melanin
CC   synthesis, fat metabolism and analgesic activity. The fusion proteins may
CC   by produced in a fungal fusion system that additionally comprise fusion
CC   partners, such as the alpha-mating factor (AMF), propeptide, human serum
CC   albumin (HSA) and any other sequence that promotes expression and
CC   secretion of the fusion protein, and subsequent cleavage (during
CC   secretion from the fungal cell) to release heterologous protein into the
```

CC culture medium. The heterologous protein is especially BLT, human
CC parathyroid hormone (hPTH) (residues 1-34) and V8-GLIP
CC (glucagon-like insulinotropic peptide) (claimed).
XX
SQ Sequence 128 AA;

AAY96847 Length: 128 January 22, 2004 18:02 Type: P Check: 3743 ..

1 MHHSGEHFEG EKVFRVNVED ENDISLLHEL ASTRQIDFWK PDSVTQIKPH

51 STVDFRVKAE DILAVEDFLE QNELQYEVLI NNLRSVLEAQ FDSLVPRHVE

101 GTFTSDVSSY LEGQAAKEFI AWLVKGRG

!!AA_SEQUENCE 1.0
ID AAY53277 standard; peptide; 31 AA.
XX
AC AAY53277;
XX
DT 24-JUL-2000 (first entry)
XX
DE Glucagon-like peptide-1 analogue #1.
XX
KW Human; glucagon-like peptide-1; GLP-1; stroke; blood glucose;
KW diabetes; non-insulin dependent diabetes; NIDDM; insulinotropic;
KW cardioactive; antidiabetic; cerebroprotective.
XX
OS Homo sapiens.
XX
PN WO200016797-A2.
XX
PD 30-MAR-2000.
XX
PF 22-SEP-1999; 99WO-US22026.
XX
PR 24-SEP-1998; 98US-0101719.
XX
PA (ELIL) LILLY & CO ELI.
XX
PI Efendic S;
XX
DR WPI; 2000-283446/24.
XX
PT Reducing mortality and morbidity following strokes by administering
PT glucagon like peptides -
XX
PS Disclosure; Page 6; 36pp; English.
XX
CC A method (I) has been developed for reducing mortality and morbidity
CC following a stroke. The method comprises administering glucagon-like
CC peptides (GLP)-1, GLP-1 analogues, GLP-1 derivatives and/or salts of
CC GLP-1, in a dose sufficient to normalise blood glucose levels. (I) may
CC be used for reducing morbidity and mortality following strokes by
CC controlling hypoglycaemia. The method is particularly suitable for
CC treating non-insulin dependent diabetes (NIDDM), those at risk of
CC stroke or those who have on-going or recurring strokes. The method
CC reduces morbidity and mortality in diabetics after strokes, for example,
CC by effecting smaller infarct size. Treatment using (I) in NIDDM compared
CC to combined treatment with infusions of insulin and glucose avoids
CC inconvenient and expensive monitoring of blood glucose as well as
CC interpretation of blood glucose results and adjustment of insulin dose
CC rate. The treatments also avoid the risk of hypoglycaemia that
CC accompanies insulin infusion. Although GLP-1 has a short half life the
CC need for continuous administration is not disadvantageous as the
CC patient is typically bed ridden in an intensive care unit where fluids
CC can be continuously administered parenterally. (I) can be used to treat
CC all patients with hypoglycaemia irrespective of whether they are
CC diagnosed as diabetic. Pre-existing hyperglycaemia is rectified and
CC new-onset hyperglycaemia is prevented. The present sequence represents
CC a GLP-1 analogue which is given in the exemplification of the present
CC invention.
XX
SQ Sequence 31 AA;

AAY53277 Length: 31 January 22, 2004 18:02 Type: P Check: 7361 ..

1 HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID AAY83149 standard; peptide; 31 AA.
XX
AC AAY83149;
XX
DT 24-JUL-2000 (first entry)
XX
DE Glucagon-like peptide-1.
XX
KW Glucagon-like peptide-1; GLP-1; treatment; pulmonary; inhalation;
KW lungs; diabetes; hyperglycaemia.
XX
OS Synthetic.
XX
PN WO200012116-A1.
XX
PD 09-MAR-2000.
XX
PF 24-AUG-1999; 99WO-US19348.
XX
PR 28-AUG-1998; 98US-0098273.
PR 11-SEP-1998; 98US-0100012.
XX
PA (ELIL) LILLY & CO ELI.
XX
PI Hughes BL, Wolff RK;
XX
DR WPI; 2000-237776/20.
XX
PT Administration of glucagon-like peptide-1 molecule by pulmonary means,
PT useful for treating diabetes and hyperglycemia
XX
PS Example 1; Page 43; 45pp; English.
XX
CC Administration of a glucagon-like peptide-1 (GLP-1) molecule by
CC inhalation can be used to treat diabetes and hyperglycaemia.
CC Analogs and derivatives of the GLP-1 molecule can also be used in
CC the treatment method. The GLP-1 molecule can be reproducibly and
CC effectively delivered through the lungs.
XX
SQ Sequence 31 AA;

AAY83149 Length: 31 January 22, 2004 18:02 Type: P Check: 7403 ..

1 HVEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID AAY78950 standard; peptide; 31 AA.
XX
AC AAY78950;
XX
DT 05-JUN-2000 (first entry)
XX
DE Glucagon-like peptide-1 fragment GLP-1 (7-37).
XX
KW Glucagon-like peptide-1; GLP-1; insulin producing cell; insulin; amylase;
KW diabetes mellitus type 1; human; livestock; pet.
XX
OS Homo sapiens.
XX
PN WO200009666-A2.
XX
PD 24-FEB-2000.
XX
PF 10-AUG-1999; 99WO-US18099.
XX
PR 10-AUG-1998; 98US-0095917.
XX

PA (USSH) US DEPT HEALTH & HUMAN SERVICES.
XX
PI Egan J, Perfetti R, Passaniti A, Greig N, Holloway H;
XX
DR WPI; 2000-205999/18.
XX
PT Differentiation of non-insulin producing cells into insulin-producing
PT cells by glucagon-like peptide-1 or extendin-4, used to treat diabetes
PT mellitus -
XX
PS Disclosure; Page 16; 119pp; English.
XX
CC This sequence represents a glucagon-like peptide-1 (GLP-1) fragment.
CC GLP-1 is a hormone normally secreted by neuroendocrine cells of the gut,
CC in response to food. GLP-1 fragments or Extendin-4 growth factor
CC fragments can be used in the production of a population of
CC insulin-producing cells from a population of non-insulin producing cells.
CC The methods may also be used to promote pancreatic amylase producing
CC cells to produce both insulin and amylase. The methods are used to treat
CC diabetes mellitus (type 1) in humans, domesticated animals, livestock and
CC pets.
XX
SQ Sequence 31 AA;

AAY78950 Length: 31 January 22, 2004 18:02 Type: P Check: 7361 ..

1 HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID AAY67372 standard; peptide; 31 AA.
XX
AC AAY67372;
XX
DT 25-APR-2000 (first entry)
XX
DE Glucagon-like peptide-1 (7-37) amino acid sequence.
XX
KW Glucagon-like peptide-1; GLP-1; enteric peptide; incretin hormone;
KW impaired glucose tolerance; insulin secretion regulator; cerebrovascular;
KW cardiovascular event; pancreatic beta-cell response.
XX
OS Mammalia sp.
XX
PN WO9964061-A1.
XX
PD 16-DEC-1999.
XX
PF 07-MAY-1999; 99WO-US10040.
XX
PR 12-JUN-1998; 98US-0089044.
XX
PA (BION-) BIONEBRASKA INC.
XX
PI Goke B, Byrne M;
XX
DR WPI; 2000-126441/11.
XX
PT Novel glucagon-like peptide-1 used to improve the pancreatic beta-cell
PT response to glucose -
XX
PS Claim 4; Page 25; 46pp; English.
XX
CC This sequence represents a glucagon-like peptide-1 (GLP-1 7-37) which is
CC used in the method of the invention. GLP-1 is a natural enteric peptide
CC secreted from the L-cells of the gut, and acts an an incretin hormone
CC stimulating pancreatic beta cells to secrete insulin in a glucose
CC dependent manner. The application of a novel GLP-1 in subjects with
CC impaired glucose tolerance (IGT) re-establishes the tightly coordinated
CC response of insulin secretion to increases in plasma glucose levels. The
CC methods, compositions and glucagon-like peptide-1 (GLP-1) of the
CC invention can be used in therapeutic treatment for normalising impaired
CC glucose tolerance. Administration of GLP-1 also regulates or normalises
CC insulin secretion patterns which will result in overall reduction of
CC plasma insulin in impaired glucose tolerance (IGT). This normalisation
CC will in turn reduce the condition of insulin resistance. The effective
CC treatment of IGT also decreases the risk of cardiovascular and
CC cerebrovascular events. It can therefore be provided as a preventative to
CC patients of known high risk for such events. Antibodies against GLP-1 can
CC be used to identify GLP-1 like peptides for use in the methods of the
CC invention.
XX
SQ Sequence 31 AA;

AAY67372 Length: 31 January 22, 2004 18:02 Type: P Check: 7361 ..

1 HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID AAY67374 standard; peptide; 37 AA.
XX
AC AAY67374;
XX
DT 25-APR-2000 (first entry)
XX
DE Glucagon-like peptide-1 (1-37) amino acid sequence.
XX
KW Glucagon-like peptide-1; GLP-1; enteric peptide; incretin hormone;
KW impaired glucose tolerance; insulin secretion regulator; cerebrovascular;
KW cardiovascular event; pancreatic beta-cell response.
XX
OS Mammalia sp.
XX
PN WO9964061-A1.
XX
PD 16-DEC-1999.
XX
PF 07-MAY-1999; 99WO-US10040.
XX
PR 12-JUN-1998; 98US-0089044.
XX
PA (BION-) BIONEBRASKA INC.
XX
PI Goke B, Byrne M;
XX
DR WPI; 2000-126441/11.
XX
PT Novel glucagon-like peptide-1 used to improve the pancreatic beta-cell
PT response to glucose -
XX
PS Disclosure; Page 9; 46pp; English.
XX
CC This sequence represents a glucagon-like peptide-1 (GLP-1 1-37) which is
CC used in the method of the invention. GLP-1 is a natural enteric peptide
CC secreted from the L-cells of the gut, and acts an an incretin hormone
CC stimulating pancreatic beta cells to secrete insulin in a glucose
CC dependent manner. The application of a novel GLP-1 in subjects with
CC impaired glucose tolerance (IGT) re-establishes the tightly coordinated
CC response of insulin secretion to increases in plasma glucose levels. The
CC methods, compositions and glucagon-like peptide-1 (GLP-1) of the
CC invention can be used in therapeutic treatment for normalising impaired
CC glucose tolerance. Administration of GLP-1 also regulates or normalises
CC insulin secretion patterns which will result in overall reduction of
CC plasma insulin in impaired glucose tolerance (IGT). This normalisation
CC will in turn reduce the condition of insulin resistance. The effective
CC treatment of IGT also decreases the risk of cardiovascular and
CC cerebrovascular events. It can therefore be provided as a preventative to
CC patients of known high risk for such events. Antibodies against GLP-1 can
CC be used to identify GLP-1 like peptides for use in the methods of the
CC invention.
XX
SQ Sequence 37 AA;

AAY67374 Length: 37 January 22, 2004 18:02 Type: P Check: 2897 ..

1 HDEFERHAEG TFTSDVSSYL EGQAAKEFIA WLVKGRG

```
!!AA_SEQUENCE 1.0
ID   ABG71251 standard; Peptide; 37 AA.
XX
AC   ABG71251;
XX
DT   16-DEC-2002  (first entry)
XX
DE   Human glucagon-like peptide-1 (GLP-1) peptide #1.
XX
KW   Glucagon-like peptide-1; GLP-1; insulinotropic response; neurotropic;
KW   ischaemia injured brain cell; insulin; neuroprotective; hypoglycaemia;
KW   stroke-related hyperglycaemia; cerebroprotective; insulin-stimulator;
KW   stroke; human.
XX
OS   Homo sapiens.
XX
PN   US6429197-B1.
XX
PD   06-AUG-2002.
XX
PF   30-APR-1999;   99US-0303016.
XX
PR   08-OCT-1998;   98US-103498P.
XX
PA   (BION-) BIONEBRASKA INC.
XX
PI   Coolidge TR,  Ehlers MRW;
XX
DR   WPI; 2002-739470/80.
XX
PT   New use of glucagon-like peptide-1 (GLP-1) to increase insulinotropic
PT   responses in ischaemia injured brain cells to treat e.g. stroke -
XX
PS   Disclosure; Column 5; 9pp; English.
XX
CC   The present invention relates to a new method for increasing
CC   insulinotropic responses in ischaemia injured brain cells. The method
CC   involves administering a composition containing glucagon-like peptide-1
CC   (GLP-1) and a carrier, where the produced insulin is neuroprotective by
CC   direct neurotropic effects and by controlling stroke-related
CC   hyperglycaemia. The method is useful for increasing insulinotropic
CC   responses in ischaemic injured brain cells e.g. caused by stroke, by
CC   promoting a neuroprotective effect. The invention can maintain mild
CC   hypoglycaemia with no risk of severe hypoglycaemia. The present amino
CC   acid sequence represents a human GLP-1 peptide as described by the
CC   invention.
XX
SQ   Sequence   37 AA;

 ABG71251  Length: 37  January 22, 2004 18:02  Type: P  Check: 2897  ..

       1  HDEFERHAEG TFTSDVSSYL EGQAAKEFIA WLVKGRG

!!AA_SEQUENCE 1.0
ID   ABG71253 standard; Peptide; 31 AA.
XX
AC   ABG71253;
XX
DT   16-DEC-2002  (first entry)
XX
DE   Human glucagon-like peptide-1 (GLP-1) peptide #2.
XX
KW   Glucagon-like peptide-1; GLP-1; insulinotropic response; neurotropic;
KW   ischaemia injured brain cell; insulin; neuroprotective; hypoglycaemia;
KW   stroke-related hyperglycaemia; cerebroprotective; insulin-stimulator;
KW   stroke; human.
XX
OS   Homo sapiens.
XX
PN   US6429197-B1.
XX
PD   06-AUG-2002.
XX
PF   30-APR-1999;   99US-0303016.
XX
PR   08-OCT-1998;   98US-103498P.
XX
PA   (BION-) BIONEBRASKA INC.
XX
PI   Coolidge TR,  Ehlers MRW;
XX
DR   WPI; 2002-739470/80.
XX
PT   New use of glucagon-like peptide-1 (GLP-1) to increase insulinotropic
PT   responses in ischaemia injured brain cells to treat e.g. stroke -
XX
PS   Disclosure; Column 5; 9pp; English.
XX
CC   The present invention relates to a new method for increasing
CC   insulinotropic responses in ischaemia injured brain cells. The method
CC   involves administering a composition containing glucagon-like peptide-1
CC   (GLP-1) and a carrier, where the produced insulin is neuroprotective by
CC   direct neurotropic effects and by controlling stroke-related
CC   hyperglycaemia. The method is useful for increasing insulinotropic
CC   responses in ischaemic injured brain cells e.g. caused by stroke, by
CC   promoting a neuroprotective effect. The invention can maintain mild
CC   hypoglycaemia with no risk of severe hypoglycaemia. The present amino
CC   acid sequence represents a human GLP-1 peptide as described by the
CC   invention.
XX
SQ   Sequence   31 AA;

 ABG71253  Length: 31  January 22, 2004 18:02  Type: P  Check: 7361  ..

       1  HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID   AAE25338 standard; peptide; 31 AA.
XX
AC   AAE25338;
XX
DT   30-OCT-2002  (first entry)
XX
DE   Human glucagon-like peptide-1 related peptide, Val8-GLP-1 (7-37) OH.
XX
KW   Human; pharmaceutical composition; diabetes; hyperglycaemia; obesity;
KW   irritable bowel syndrome; glucagon-like peptide-1 related peptide;
KW   Val8-GLP-1 (7-37) OH; anorectic; antiinflammatory.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
PN   WO200247715-A2.
XX
PD   20-JUN-2002.
XX
PF   06-DEC-2001; 2001WO-US43188.
XX
PR   13-DEC-2000; 2000US-255251P.
XX
PA   (ELIL ) LILLY & CO ELI.
XX
PI   Dodd SW,  Rinella JVJ,  Watts EA,  Ng K;
XX
DR   WPI; 2002-519754/55.
XX
PT   Pharmaceutical composition useful in the treatment of e.g. diabetes
PT   comprises crystals of peptide, glycine, zinc, alcohol, a buffer and a
PT   preservative  -
XX
PS   Example 1; Page 68; 68pp; English.
XX
CC   The invention relates to a pharmaceutical composition which comprises
CC   crystals of a peptide, glycine, zinc, alcohol, a buffer and a
CC   preservative. The invention is used in the manufacture of a medicament
CC   for the treatment of diabetes, hyperglycaemia and obesity in a mammal;
```

CC for treating human or animal by therapy. The invention is also used for
CC treating irritable bowel syndrome. The present sequence is a human
CC glucagon-like peptide-1 related peptide, Val8-(GLP-1 (7-37) OH).
XX
SQ Sequence 31 AA;

AAE25338 Length: 31 January 22, 2004 18:02 Type: P Check: 7403 ..

1 HVEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID AAE25339 standard; peptide; 31 AA.
XX
AC AAE25339;
XX
DT 30-OCT-2002 (first entry)
XX
DE Human glucagon-like peptide-1 related peptide GLP-1 (7-37) OH.
XX
KW Human; pharmaceutical composition; diabetes; hyperglycaemia; obesity;
KW irritable bowel syndrome; glucagon-like peptide-1 related peptide;
KW GLP-1 (7-37) OH; anorectic; antiinflammatory.
XX
OS Homo sapiens.
OS Synthetic.
XX
PN WO200247715-A2.
XX
PD 20-JUN-2002.
XX
PF 06-DEC-2001; 2001WO-US43188.
XX
PR 13-DEC-2000; 2000US-255251P.
XX
PA (ELIL) LILLY & CO ELI.
XX
PI Dodd SW, Rinella JVJ, Watts EA, Ng K;
XX
DR WPI; 2002-519754/55.
XX
PT Pharmaceutical composition useful in the treatment of e.g. diabetes
PT comprises crystals of peptide, glycine, zinc, alcohol, a buffer and a
PT preservative -
XX
PS Disclosure; Page 68; 68pp; English.
XX
CC The invention relates to a pharmaceutical composition which comprises
CC crystals of a peptide, glycine, zinc, alcohol, a buffer and a
CC preservative. The invention is used in the manufacture of a medicament
CC for the treatment of diabetes, hyperglycaemia and obesity in a mammal;
CC for treating human or animal by therapy. The invention is also used for
CC treating irritable bowel syndrome. The present sequence is a human
CC glucagon-like peptide-1 related peptide (GLP-1 (7-37) OH).
XX
SQ Sequence 31 AA;

AAE25339 Length: 31 January 22, 2004 18:02 Type: P Check: 7361 ..

1 HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID AAO22093 standard; Peptide; 31 AA.
XX
AC AAO22093;
XX
DT 11-OCT-2002 (first entry)
XX
DE Glucagon-like peptide-1 (GLP-1), SEQ ID No 7.
XX
KW Antidiabetic; anorectic; crystal; diabetes; hyperglycaemia; obesity;
KW glucagon-like peptide-1; GLP-1.
XX
OS Synthetic.
XX
PN WO200248183-A2.
XX
PD 20-JUN-2002.
XX
PF 06-DEC-2001; 2001WO-US43183.
XX
PR 13-DEC-2000; 2000US-255251P.
XX
PA (ELIL) LILLY & CO ELI.
XX
PI Dodd SW, Millican RL, Rinella JVJ;
XX
DR WPI; 2002-557606/59.
XX
PT New peptide crystals useful in the treatment of e.g. diabetes -
XX
PS Claim 1; Page 14; 103pp; English.
XX
CC The invention relates to the provision of novel crystals of selected
CC peptides and compositions thereof. The invention also provides stable
CC pharmaceutical compositions comprising crystals of selected peptide,
CC glycine, an alcohol, zinc, a buffer and a pharmaceutically acceptable
CC preservative at a pH of about 6.0 to about 8.5. The novel crystals are
CC useful in the preparation of a medicament for the treatment of diabetes,
CC hyperglycaemia and obesity. The novel peptides have a reduced propensity
CC to self-associate or aggregate, and exhibits satisfactory chemical and
CC physical stability. This sequence represents a glucagon-like peptide-1
CC (GLP-1) relating to the novel crystals of the invention.
XX
SQ Sequence 31 AA;

AAO22093 Length: 31 January 22, 2004 18:02 Type: P Check: 7361 ..

1 HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID ABB80094 standard; peptide; 37 AA.
XX
AC ABB80094;
XX
DT 02-OCT-2002 (first entry)
XX
DE Glucagon like peptide-1 (GLP-1) 1-37.
XX
KW Glucagon like peptide-1; GLP-1; GLP-1 (1-37); cardiant; antidiabetic;
KW vasotropic; hibernating myocardium; congestive heart failure;
KW ischaemic cardiomyopathy; diabetic cardiomyopathy.
XX
OS Mammalia.
XX
PN WO200234285-A2.
XX
PD 02-MAY-2002.
XX
PF 22-OCT-2001; 2001WO-US32559.
XX
PR 20-OCT-2000; 2000US-241834P.
PR 23-OCT-2000; 2000US-242139P.
PR 03-NOV-2000; 2000US-245234P.
XX
PA (COOL/) COOLIDGE T R.
XX
PI Ehlers M;
XX
DR WPI; 2002-426545/45.
XX
PT Treatment of hibernating myocardium involves administering GLP-1
PT molecule -
XX
PS Disclosure; Page 7; 25pp; English.
XX
CC The invention relates to the treatment of hibernating myocardium by

```
CC   administering a GLP-1 (glucagon like peptide-1) molecule. GLP-1 activity
CC   may be described as, cardiant, antidiabetic and vasotropic. GLP-1 may be
CC   used for treating, hibernating myocardium, congestive heart failure,
CC   ischaemic cardiomyopathy and diabetic cardiomyopathy. GLP-1 reduces
CC   plasma or heart norepinepherine level in a patient. The current sequence
CC   represents glucagon like peptide-1 (GLP-1) 1-37.
XX
SQ   Sequence   37 AA;

 ABB80094  Length: 37  January 22, 2004 18:02  Type: P  Check: 2897  ..

       1  HDEFERHAEG TFTSDVSSYL EGQAAKEFIA WLVKGRG

!!AA_SEQUENCE 1.0
ID   ABB80096 standard; peptide; 31 AA.
XX
AC   ABB80096;
XX
DT   02-OCT-2002  (first entry)
XX
DE   Glucagon like peptide-1 (GLP-1) 7-37.
XX
KW   Glucagon like peptide-1; GLP-1; GLP-1 (7-37); cardiant; antidiabetic;
KW   vasotropic; hibernating myocardium; congestive heart failure;
KW   ischaemic cardiomyopathy; diabetic cardiomyopathy.
XX
OS   Mammalia.
XX
PN   WO200234285-A2.
XX
PD   02-MAY-2002.
XX
PF   22-OCT-2001; 2001WO-US32559.
XX
PR   20-OCT-2000; 2000US-241834P.
PR   23-OCT-2000; 2000US-242139P.
PR   03-NOV-2000; 2000US-245234P.
XX
PA   (COOL/) COOLIDGE T R.
XX
PI   Ehlers M;
XX
DR   WPI; 2002-426545/45.
XX
PT   Treatment of hibernating myocardium involves administering GLP-1
PT   molecule -
XX
PS   Disclosure; Page 7; 25pp; English.
XX
CC   The invention relates to the treatment of hibernating myocardium by
CC   administering a GLP-1 (glucagon like peptide-1) molecule. GLP-1 activity
CC   may be described as, cardiant, antidiabetic and vasotropic. GLP-1 may be
CC   used for treating, hibernating myocardium, congestive heart failure,
CC   ischaemic cardiomyopathy and diabetic cardiomyopathy. GLP-1 reduces
CC   plasma or heart norepinepherine level in a patient. The current sequence
CC   represents glucagon like peptide-1 (GLP-1) 7-37, which is produced from
CC   the enzymatical processing of GLP-1 (1-37) (see ABB80094).
XX
SQ   Sequence   31 AA;

 ABB80096  Length: 31  January 22, 2004 18:02  Type: P  Check: 7361  ..

       1  HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID   ABB80861 standard; peptide; 31 AA.
XX
AC   ABB80861;
XX
DT   08-OCT-2002  (first entry)
XX
DE   Human glucagon-like peptide-1 (GLP-1) related peptide GLP-1 (7-37)OH.
XX
KW   Glucagon-like peptide; GLP; GLP-1; antidiabetic; antiinflammatory;
KW   cardiant; cerebroprotective; anorectic; human.
XX
OS   Homo sapiens.
XX
PN   WO200248192-A2.
XX
PD   20-JUN-2002.
XX
PF   30-NOV-2001; 2001WO-US43167.
XX
PR   13-DEC-2000; 2000US-255251P.
XX
PA   (ELIL ) LILLY & CO ELI.
XX
PI   Millican RLJ,  Glaesner W,  Dimarchi RD;
XX
DR   WPI; 2002-557607/59.
XX
PT   New amidated glucagon-like peptide useful for the treatment of e.g.
PT   diabetes -
XX
PS   Disclosure; Page 4; 50pp; English.
XX
CC   The invention provides an amidated glucagon-like peptide (GLP-1) with the
CC   sequence as shown in ABB80860. The amidated GLP-1 peptide, crystals of
CC   the peptide, pharmaceutical compositions comprising the crystals or the
CC   peptide are all useful in the manufacture of a medicament for the
CC   treatment of diabetes, hyperglycemia, obesity, for the reduction of
CC   morbidity and mortality associated with myocardial infarction or stroke,
CC   for the attenuation of catabolic changes that occur after surgery, in a
CC   mammal (preferably human and animal). They are also useful for treatment
CC   of irritable bowel syndrome. The present sequence represents a naturally
CC   occuring human GLP-1 related peptide GLP-1(7-37)OH.
XX
SQ   Sequence   31 AA;

 ABB80861  Length: 31  January 22, 2004 18:02  Type: P  Check: 7361  ..

       1  HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID   ABB80862 standard; peptide; 31 AA.
XX
AC   ABB80862;
XX
DT   08-OCT-2002  (first entry)
XX
DE   Glucagon-like peptide-1 (GLP-1) Val8-GLP-1(7-37)NH2.
XX
KW   Glucagon-like peptide; GLP; GLP-1; antidiabetic; antiinflammatory;
KW   cardiant; cerebroprotective; anorectic.
XX
OS   Synthetic.
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 2
FT                   /label= A8V
FT                   /note= "Ala is substituted with Val"
FT   Modified-site   31
FT                   /note= "C-terminal amide"
XX
PN   WO200248192-A2.
XX
PD   20-JUN-2002.
XX
PF   30-NOV-2001; 2001WO-US43167.
XX
PR   13-DEC-2000; 2000US-255251P.
XX
PA   (ELIL ) LILLY & CO ELI.
XX
```

PI Millican RLJ, Glaesner W, Dimarchi RD;
XX
DR WPI; 2002-557607/59.
XX
PT New amidated glucagon-like peptide useful for the treatment of e.g.
PT diabetes -
XX
PS Disclosure; Page 4; 50pp; English.
XX
CC The invention provides an amidated glucagon-like peptide (GLP-1) with the
CC sequence as shown in ABB80860. The amidated GLP-1 peptide, crystals of
CC the peptide, pharmaceutical compositions comprising the crystals or the
CC peptide are all useful in the manufacture of a medicament for the
CC treatment of diabetes, hyperglycemia, obesity, for the reduction of
CC morbidity and mortality associated with myocardial infarction or stroke,
CC for the attenuation of catabolic changes that occur after surgery, in a
CC mammal (preferably human and animal). They are also useful for treatment
CC of irritable bowel syndrome. The present sequence represents an amidated
CC GLP-1 peptide Val8-GLP(7-37)NH2.
XX
SQ Sequence 31 AA;

ABB80862 Length: 31 January 22, 2004 18:02 Type: P Check: 7403 ..

1 HVEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID AAU85972 standard; peptide; 31 AA.
XX
AC AAU85972;
XX
DT 21-MAY-2002 (first entry)
XX
DE Modified human glucagon-like peptide 1 (hGLP-1) residues 7-37.
XX
KW Increased biological potency; prolonged activity; increased half-life;
KW glucose intolerance; insulin resistance; type II diabetes; bone disease;
KW cancer; inflammatory disorder; obesity; developmental disorder;
KW hyperproliferative skin disease; hormone-dependent disease; homeostasis;
KW intestinal disease; interleukin-8 production; smooth muscle contraction;
KW feeding; blood pressure; pancreatic secretion; mutant; mutein; human;
KW glucagon-like peptide 1; hGLP-1.
XX
OS Homo sapiens.
OS Synthetic.
XX
FH Key Location/Qualifiers
FT Modified-site 31
FT /note= "Optionally modified by C-terminal amide"
XX
PN WO200210195-A2.
XX
PD 07-FEB-2002.
XX
PF 02-AUG-2001; 2001WO-CA01119.
XX
PR 02-AUG-2000; 2000US-222619P.
XX
PA (THER-) THERATECHNOLOGIES INC.
XX
PI Gravel D, Habi A, Abribat T;
XX
DR WPI; 2002-206179/26.
XX
PT Novel modified biological peptide with increased biological potency,
PT prolonged activity, increased half-life, for treating glucose
PT intolerance associated or not with insulin resistance pathologies, type
PT II diabetes -
XX
PS Claim 5; Page 53; 77pp; English.
XX
CC The present invention relates to modified biological peptides with
CC increased biological potency, prolonged activity and/or increased
CC half-life. The peptides of the invention are useful in the treatment
CC of glucose intolerance which may be associated with insulin resistance
CC pathologies, and in the treatment of type II diabetes. They are also
CC useful for treating bone diseases, cancer, diseases related to
CC inflammatory responses, obesity, autism, pervasive developmental
CC disorders, hyperproliferative skin diseases, hormone-dependent diseases,
CC They can be used for regulating blood glucose, enhancing mucosal
CC regeneration in patients with intestinal diseases, inhibition of
CC interleukin-8 production, stimulation of acid release, homeostasis,
CC regulation of exocrine and endocrine secretions, smooth muscle
CC contraction, feeding, blood pressure, body temperature and cell growth,
CC regulation of food intake and energy balance, and stimulation of
CC pancreatic secretion or cell growth. AAU85971-AAU86019 represent the
CC modified biological peptides of the invention.
XX
SQ Sequence 31 AA;

AAU85972 Length: 31 January 22, 2004 18:02 Type: P Check: 7361 ..

1 HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID AAE17659 standard; peptide; 31 AA.
XX
AC AAE17659;
XX
DT 01-MAY-2002 (first entry)
XX
DE Glucagon-like peptide-1 (GLP-1) peptide, GLP-1(7-37).
XX
KW Glucagon-like peptide-1; GLP-1; obesity; stroke; myocardial infarction;
KW catabolic change; irritable bowel syndrome; therapy; diabetes; dyspepsia;
KW impaired glucose tolerance; impaired fasting glucose; gastrointestinal;
KW partial pancreatectomy; pancreatitis; anorectic; antidiabetic; cardiant;
KW antiinflammatory; cerebroprotective.
XX
OS Unidentified.
XX
PN WO200198331-A2.
XX
PD 27-DEC-2001.
XX
PF 01-JUN-2001; 2001WO-US16474.
XX
PR 16-JUN-2000; 2000US-212171P.
PR 13-OCT-2000; 2000US-240349P.
XX
PA (ELIL) LILLY & CO ELI.
XX
PI Glaesner W, Millican RL;
XX
DR WPI; 2002-075625/10.
XX
PT Modified glucagon-like peptide-1 compounds, useful for treating
PT disorders associated with need for stimulation of glucagon-like
PT peptide-1 receptor e.g. obesity, stroke or myocardial infarction -
XX
PS Example 4; Page 8; 69pp; English.
XX
CC The present invention relates to glucagon-like peptide-1 (GLP-1)
CC compound and its analogues. The invention is used for stimulating the
CC glucagon-like peptide-1 (GLP-1) receptor and for treatment or preparation
CC of a medicament for treatment of disorders where stimulation of the GLP-1
CC receptor is needed, such as obesity, stroke, myocardial infarction,
CC catabolic changes after surgery or irritable bowel syndrome. GLP-1 is
CC also used for preparation of a medicament for prophylactic treatment of
CC non-insulin dependent diabetes and insulin dependent diabetes. Also for
CC treating functional dyspepsia, impaired glucose tolerance, impaired
CC fasting glucose, partial pancreatectomy, gestational diabetes and acute
CC or chronic pancreatitis. The present sequence is GLP-1.
XX
SQ Sequence 31 AA;

AAE17659 Length: 31 January 22, 2004 18:02 Type: P Check: 7361 ..

1 HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

```
!!AA_SEQUENCE 1.0
ID   AAE17694 standard; peptide; 31 AA.
XX
AC   AAE17694;
XX
DT   01-MAY-2002  (first entry)
XX
DE   Glucagon-like peptide-1 (GLP-1) analogue, Val8-GLP-1(7-37).
XX
KW   Glucagon-like peptide-1; GLP-1; obesity; stroke; myocardial infarction;
KW   catabolic change; irritable bowel syndrome; therapy; diabetes; dyspepsia;
KW   impaired glucose tolerance; impaired fasting glucose; gastrointestinal;
KW   partial pancreatectomy; pancreatitis; anorectic; antidiabetic; cardiant;
KW   antiinflammatory; cerebroprotective.
XX
OS   Unidentified.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 2
FT                   /note= "Wild type Ala substituted with Val"
XX
PN   WO200198331-A2.
XX
PD   27-DEC-2001.
XX
PF   01-JUN-2001; 2001WO-US16474.
XX
PR   16-JUN-2000; 2000US-212171P.
PR   13-OCT-2000; 2000US-240349P.
XX
PA   (ELIL ) LILLY & CO ELI.
XX
PI   Glaesner W,  Millican RL;
XX
DR   WPI; 2002-075625/10.
XX
PT   Modified glucagon-like peptide-1 compounds, useful for treating
PT   disorders associated with need for stimulation of glucagon-like
PT   peptide-1 receptor e.g. obesity, stroke or myocardial infarction -
XX
PS   Example 4; Page -; 69pp; English.
XX
CC   The present invention relates to glucagon-like peptide-1 (GLP-1)
CC   compound and its analogues. The invention is used for stimulating the
CC   glucagon-like peptide-1 (GLP-1) receptor and for treatment or preparation
CC   of a medicament for treatment of disorders where stimulation of the GLP-1
CC   receptor is needed, such as obesity, stroke, myocardial infarction,
CC   catabolic changes after surgery or irritable bowel syndrome. GLP-1 is
CC   also used for preparation of a medicament for prophylactic treatment of
CC   non-insulin dependent diabetes and insulin dependent diabetes. Also for
CC   treating functional dyspepsia, impaired glucose tolerance, impaired
CC   fasting glucose, partial pancreatectomy, gestational diabetes and acute
CC   or chronic pancreatitis. The present sequence is GLP-1 analogue.
CC   Note: The present sequence is not shown in the specification, but is
CC   derived from SEQ ID NO:19 (AAE17659) shown in page 8 of the
CC   specification.
XX
SQ   Sequence   31 AA;
```

AAE17694 Length: 31 January 22, 2004 18:02 Type: P Check: 7403 ..

1 HVEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

```
!!AA_SEQUENCE 1.0
ID   AAE14419 standard; peptide; 37 AA.
XX
AC   AAE14419;
XX
DT   26-MAR-2002  (first entry)
XX
DE   Mammalian glucagon-like peptide-1, GLP-1(1-37).
XX
KW   Acute coronary syndrome; ACS; Q-wave myocardial infarction; Q-wave MI;
KW   angina; non-Q-wave cardiac necrosis; ischaemic heart disease;
KW   congestive heart failure; heart murmur; troponin I; troponin T;
KW   creatine kinase myocardial isoenzyme; CK-MB; ST-segment; chest pain;
KW   nausea; palpitation; dizziness; angioplasty; pulmonary oedema;
KW   peripheral oedema; extrasystole; arterial fibrillation; arrhythmia;
KW   diabetes; hypertension; hypercholesterolaemia; hyperlipidaemia; obesity;
KW   smoking; impaired glucose tolerance; blood glucose; thrombolytic therapy;
KW   cardiac distress; glucagon-like peptide-1; GLP-1(1-37).
XX
OS   Mammalia.
XX
PN   WO200189554-A2.
XX
PD   29-NOV-2001.
XX
PF   18-MAY-2001; 2001WO-US15996.
XX
PR   19-MAY-2000; 2000US-205239P.
XX
PA   (BION-) BIONEBRASKA INC.
XX
PI   Coolidge TR,  Ehlers M;
XX
DR   WPI; 2002-089892/12.
XX
PT   New method of treating patients suffering from acute coronary syndrome,
PT   but not suffering from Q-wave myocardial infarction involves the use of
PT   glucagon-like peptide-1 derivatives -
XX
PS   Disclosure; Page 10; 38pp; English.
XX
CC   The invention relates to a novel method of treating patients suffering
CC   from acute coronary syndrome (ACS) and not from Q-wave myocardial
CC   infarction (Q-wave MI) that involves administering a glucagon-like
CC   peptide-1 (GLP-1) molecule to the patients. The method is also useful for
CC   treating patients suffering from stable/unstable angina, non-Q-wave
CC   cardiac necrosis, ischaemic heart disease or at a risk of developing
CC   ischaemic heart disease, cardiac abnormalities including congestive
CC   heart failure, worsening heart murmur (due to mitral regurgitation and
CC   cardiac conduction disturbances); for treating patients who have
CC   a blood troponin I level of less than 0.4 ng/ml and blood troponin T
CC   level of no more than 0.1 ng/ml; do not have elevated blood creatine
CC   kinase myocardial enzyme and ST-segment elevation, do not exhibit a
CC   pathological Q-wave, exhibit pain or symptoms such as chest pain greater
CC   than 15 minutes in duration, chest pain at rest or chest pain following
CC   minimal exertion (that is poorly responsive to sublingual nitrates),
CC   nausea, shortness of breath, palpitation and dizziness and have not
CC   suffered from a Q-wave myocardial infarction prior to the onset of the
CC   symptoms, and having normal ECG. The GLP-1 compound is further
CC   useful in angioplasty, for treating patients showing
CC   symptoms of pulmonary and peripheral oedema, atrial or ventricular
CC   extrasystoles, arterial fibrillation and other arrhythmias; and those
CC   suffering from diabetes, hypertension, hypercholesterolaemia,
CC   hyperlipidaemia, obesity and smoking. The administration of GLP-1
CC   following a Q-myocardial infarction (QMI) ameliorates the tissue damage
CC   that results from the QMI and subsequent reperfusion-induced injury. An
CC   advantage of using GLP-1 molecules is that high doses can be used without
CC   consequent hypoglycaemia and hyperglycaemia. Thus doses up to 10 nmol/kg
CC   can be used without adverse effects, as the action of the molecules are
CC   ideal for optimising glucose metabolism in individuals including those
CC   with impaired glucose tolerance and elevated or aberrant blood glucose
CC   levels. The molecule increases the time during which thrombolytic
CC   therapy becomes effective following the first symptom of cardiac
CC   distress. The present sequence is mammalian GLP-1(1-37) peptide
CC   used in the invention.
XX
SQ   Sequence   37 AA;
```

AAE14419 Length: 37 January 22, 2004 18:02 Type: P Check: 2897 ..

1 HDEFERHAEG TFTSDVSSYL EGQAAKEFIA WLVKGRG

```
!!AA_SEQUENCE 1.0
ID   AAE14421 standard; peptide; 31 AA.
XX
AC   AAE14421;
XX
DT   26-MAR-2002  (first entry)
XX
DE   Mammalian glucagon-like peptide-1, GLP-1(7-37).
XX
KW   Acute coronary syndrome; ACS; Q-wave myocardial infarction; Q-wave MI;
KW   angina; non-Q-wave cardiac necrosis; ischaemic heart disease;
KW   congestive heart failure; heart murmur; troponin I; troponin T;
KW   creatine kinase myocardial isoenzyme; CK-MB; ST-segment; chest pain;
KW   nausea; palpitation; dizziness; angioplasty; pulmonary oedema;
KW   peripheral oedema; extrasystole; arterial fibrillation; arrhythmia;
KW   diabetes; hypertension; hypercholesterolaemia; hyperlipidaemia; obesity;
KW   smoking; impaired glucose tolerance; blood glucose; thrombolytic therapy;
KW   cardiac distress; glucagon-like peptide-1; GLP-1(7-37).
XX
OS   Mammalia.
XX
PN   WO200189554-A2.
XX
PD   29-NOV-2001.
XX
PF   18-MAY-2001; 2001WO-US15996.
XX
PR   19-MAY-2000; 2000US-205239P.
XX
PA   (BION-) BIONEBRASKA INC.
XX
PI   Coolidge TR,  Ehlers M;
XX
DR   WPI; 2002-089892/12.
XX
PT   New method of treating patients suffering from acute coronary syndrome,
PT   but not suffering from Q-wave myocardial infarction involves the use of
PT   glucagon-like peptide-1 derivatives -
XX
PS   Disclosure; Page 10; 38pp; English.
XX
CC   The invention relates to a novel method of treating patients suffering
CC   from acute coronary syndrome (ACS) and not from Q-wave myocardial
CC   infarction (Q-wave MI) that involves administering a glucagon-like
CC   peptide-1 (GLP-1) molecule to the patients. The method is also useful for
CC   treating patients suffering from stable/unstable angina, non-Q-wave
CC   cardiac necrosis, ischaemic heart disease or at a risk of developing
CC   ischaemic heart disease, cardiac abnormalities including congestive
CC   heart failure, worsening heart murmur (due to mitral regurgitation and
CC   cardiac conduction disturbances); for treating patients who have
CC   a blood troponin I level of less than 0.4 ng/ml and blood troponin T
CC   level of no more than 0.1 ng/ml; do not have elevated blood creatine
CC   kinase myocardial enzyme and ST-segment elevation, do not exhibit a
CC   pathological Q-wave, exhibit pain or symptoms such as chest pain greater
CC   than 15 minutes in duration, chest pain at rest or chest pain following
CC   minimal exertion (that is poorly responsive to sublingual nitrates),
CC   nausea, shortness of breath, palpitation and dizziness and have not
CC   suffered from a Q-wave myocardial infarction prior to the onset of the
CC   symptoms, and having normal ECG. The GLP-1 compound is further
CC   useful in angioplasty, for treating patients showing
CC   symptoms of pulmonary and peripheral oedema, atrial or ventricular
CC   extrasystoles, arterial fibrillation and other arrhythmias; and those
CC   suffering from diabetes, hypertension, hypercholesterolaemia,
CC   hyperlipidaemia, obesity and smoking. The administration of GLP-1
CC   following a Q-myocardial infarction (QMI) ameliorates the tissue damage
CC   that results from the QMI and subsequent reperfusion-induced injury. An
CC   advantage of using GLP-1 molecules is that high doses can be used without
CC   consequent hypoglycaemia and hyperglycaemia. Thus doses up to 10 nmol/kg
CC   can be used without adverse effects, as the action of the molecules are
CC   ideal for optimising glucose metabolism in individuals including those
CC   with impaired glucose tolerance and elevated or aberrant blood glucose
CC   levels. The molecule increases the time during which thrombolytic
CC   therapy becomes effective following the first symptom of cardiac
CC   distress. The present sequence is mammalian GLP-1(7-37) peptide
CC   used in the invention. The present peptide is produced by enzymatic
CC   processing of GLP-1(1-37).
XX
SQ   Sequence   31 AA;
```

AAE14421 Length: 31 January 22, 2004 18:02 Type: P Check: 7361 ..

1 HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

```
!!AA_SEQUENCE 1.0
ID   ABB07146 standard; peptide; 31 AA.
XX
AC   ABB07146;
XX
DT   13-MAR-2002  (first entry)
XX
DE   Glucagon-like peptide-1 (GLP-1) fragment (residues 7-37).
XX
KW   GLP-1; glucagon-like-peptide-1; growth-hormone releasing factor; GRF;
KW   parathyroid hormone; PTH; antidiabetic; anoretic; cerebroprotective;
KW   vasotropic; anti-inflammatory; antiarteriosclerotic; hepatotropic;
KW   tranquilizer; vulnerary; osteopathic; pharmaceutical.
XX
OS   Homo sapiens.
XX
PN   WO200187322-A2.
XX
PD   22-NOV-2001.
XX
PF   17-MAY-2001; 2001WO-US15872.
XX
PR   17-MAY-2000; 2000US-205377P.
PR   19-MAY-2000; 2000US-205262P.
XX
PA   (BION-) BIONEBRASKA INC.
XX
PI   Holmquist B,  Dormady DC;
XX
DR   WPI; 2002-082941/11.
XX
PT   New peptide formulation for treating disease e.g. diabetes, obesity,
PT   ischemia comprises peptides, an acid having a specified dissociation
PT   constant and an excipient  -
XX
PS   Disclosure; Page 10; 34pp; English.
XX
CC   The invention provides a pharmaceutical composition that comprises a
CC   molecule selected from a glucagon-like-peptide-1 (GLP-1) molecule, growth
CC   -hormone releasing factor (GRF) molecule or a parathyroid hormone (PTH)
CC   molecule. The composition further includes a weak acid such as acetic
CC   acid. The pH of the composition is 3 - 5. The composition can be used for
CC   the treatment of a disease or condition selected from diabetes, excess
CC   appetite, obesity, stroke, ischemia, reperfusion injury, disturbed
CC   glucose metabolism, surgery, coma, shock, gastrointestinal disease,
CC   digestive hormone disease, atherosclerosis, vascular disease, gestational
CC   diabetes, liver disease and cirrhosis, glucocorticoid excess, Cushing's
CC   disease, the presence of activated counter regulatory hormones that occur
CC   after trauma or a disease, hypertriglyceridemia, chronic pancreatitis,
CC   the need for parenteral feeding, and a catabolic state following surgery
CC   or injury. The present sequence represents a GLP-1 peptide fragment.
XX
SQ   Sequence   31 AA;
```

ABB07146 Length: 31 January 22, 2004 18:02 Type: P Check: 7361 ..

1 HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

```
!!AA_SEQUENCE 1.0
ID   AAM50391 standard; Peptide; 37 AA.
```

XX
AC AAM50391;
XX
DT 18-FEB-2002 (first entry)
XX
DE Glucagon-like peptide 1.
XX
KW Glucagon-like peptide 1; GLP-1; human; glycaemia; antidiabetic;
KW insulinotropic; non-insulin dependent diabetes mellitus; NIDDM;
KW therapy.
XX
OS Homo sapiens.
XX
PN US6284727-B1.
XX
PD 04-SEP-2001.
XX
PF 07-JUN-1995; 95US-0472349.
XX
PR 25-JAN-1994; 94US-0181655.
PR 07-APR-1993; 93US-0044133.
XX
PA (SCIO-) SCIOS INC.
XX
PI Kim Y, Lambert WJ, Qi H, Gelfand RA, Geoghegan KF, Danley DE;
XX
DR WPI; 2002-033119/04.
XX
PT Compositions useful in treatment of non-insulin dependent diabetes
PT mellitus comprises peptides and polymer e.g. polysaccharide or
PT vegetable oil -
XX
PS Claim 1(i)(b); Column 47; 42pp; English.
XX
CC The present sequence is that of glucagon-like peptide 1 (GLP-1).
CC During processing in the pancreas and intestine, GLP-1 is converted
CC to a 31-amino acid peptide comprising amino acids 7-37 of GLP-1,
CC designated GLP-1 (7-37) (see AAM50392). This peptide has
CC insulinotropic activity, i.e. it is able to stimulate, or cause to
CC be stimulated, the synthesis or expression of insulin. GLP-1
CC (7-37) is alternatively known as insulinotropin. GLP-1 and its
CC derivatives (see AAM50392-97) are used in claimed compositions
CC for prolonged administration in the treatment of non-insulin
CC dependent diabetes mellitus. The compositions, which also include
CC a polymer such as a polysaccharide or vegetable oil, enhance
CC insulin action to achieve sustained glycaemic control.
XX
SQ Sequence 37 AA;

AAM50391 Length: 37 January 22, 2004 18:02 Type: P Check: 2897 ..

1 HDEFERHAEG TFTSDVSSYL EGQAAKEFIA WLVKGRG

!!AA_SEQUENCE 1.0
ID AAM50392 standard; Peptide; 31 AA.
XX
AC AAM50392;
XX
DT 18-FEB-2002 (first entry)
XX
DE Glucagon-like peptide 1 (7-37).
XX
KW Glucagon-like peptide 1 (7-37); GLP-1 (7-37); insulinotropin;
KW human; glycaemia; antidiabetic; insulinotropic; NIDDM;
KW non-insulin dependent diabetes mellitus; therapy.
XX
OS Homo sapiens.
XX
PN US6284727-B1.
XX
PD 04-SEP-2001.
XX
PF 07-JUN-1995; 95US-0472349.
XX
PR 25-JAN-1994; 94US-0181655.
PR 07-APR-1993; 93US-0044133.
XX
PA (SCIO-) SCIOS INC.
XX
PI Kim Y, Lambert WJ, Qi H, Gelfand RA, Geoghegan KF, Danley DE;
XX
DR WPI; 2002-033119/04.
XX
PT Compositions useful in treatment of non-insulin dependent diabetes
PT mellitus comprises peptides and polymer e.g. polysaccharide or
PT vegetable oil -
XX
PS Claim 1(i)(a); Column 47; 42pp; English.
XX
CC The present sequence is that of amino acids 7-37 of glucagon-like
CC peptide 1 (GLP-1). During processing in the pancreas and
CC intestine, 37-amino acid GLP-1 is converted to 31-amino acid
CC GLP-1 (7-37). This peptide has insulinotropic activity, i.e. it is
CC able to stimulate, or cause to be stimulated, the synthesis or
CC expression of insulin. GLP-1 (7-37) is alternatively known as
CC insulinotropin. GLP-1 (7-37) and its derivatives (see AAM50393-97)
CC are used in claimed compositions for prolonged administration in
CC the treatment of non-insulin dependent diabetes mellitus. The
CC compositions, which also include a polymer such as a polysaccharide
CC or vegetable oil, enhance insulin action to achieve sustained
CC glycaemic control.
XX
SQ Sequence 31 AA;

AAM50392 Length: 31 January 22, 2004 18:02 Type: P Check: 7361 ..

1 HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID AAU07372 standard; peptide; 37 AA.
XX
AC AAU07372;
XX
DT 18-DEC-2001 (first entry)
XX
DE Mammalian glucagon-like peptide-1, GLP-1(1-37).
XX
KW Antidiarrhoeic; antiinflammatory; antiaddictive; premedication;
KW antro-duodenal motility; glucagon-like peptide-1; GLP-1; endoscopy;
KW diarrhoea; post-operative dumping syndrome; irritable bowel syndrome;
KW narcotics withdrawal.
XX
OS Homo sapiens.
XX
PN WO200168112-A2.
XX
PD 20-SEP-2001.
XX
PF 14-MAR-2001; 2001WO-EP02882.
XX
PR 14-MAR-2000; 2000US-189091P.
XX
PA (GOEK/) GOEKE B.
PA (SCHI/) SCHIRRA J.
XX
PI Goeke B, Schirra J;
XX
DR WPI; 2001-596887/67.
XX
PT Inhibiting antro-duodenal motility, useful to prevent or treat
PT gastrointestinal disorders such as irritable bowel syndrome and
PT non-infectious diarrhoea, comprises administering glucagon-like peptide
PT -
XX
PS Disclosure; Page 7; 43pp; English.
XX

CC The invention relates to a method of inhibiting antro-duodenal motility
CC in a patient, comprising administering a glucagon-like peptide (GLP-1)
CC molecule. The method is used to premedicate or in endoscopic
CC procedures or to treat or prevent non-infectious acute and chronic
CC diarrhoea, post-operative dumping syndrome, irritable bowel syndrome or
CC symptoms associated with narcotics withdrawal. Unlike prior art treatment
CC with glucagon, the invention is not contraindicated in persons with
CC diabetes, does not incur the risks of side effects such as nausea, and is
CC not expensive. The present sequence represents mammalian glucagon-like
CC peptide-1, GLP-1 (1-37), as described in the method of the invention.
XX
SQ Sequence 37 AA;

AAU07372 Length: 37 January 22, 2004 18:02 Type: P Check: 2897 ..

1 HDEFERHAEG TFTSDVSSYL EGQAAKEFIA WLVKGRG

!!AA_SEQUENCE 1.0
ID AAU07374 standard; peptide; 31 AA.
XX
AC AAU07374;
XX
DT 18-DEC-2001 (first entry)
XX
DE Mammalian glucagon-like peptide-1, GLP-1(7-37).
XX
KW Antidiarrhoeic; antiinflammatory; antiaddictive; premedication;
KW antro-duodenal motility; glucagon-like peptide-1; GLP-1; endoscopy;
KW diarrhoea; post-operative dumping syndrome; irritable bowel syndrome;
KW narcotics withdrawal.
XX
OS Homo sapiens.
XX
PN WO200168112-A2.
XX
PD 20-SEP-2001.
XX
PF 14-MAR-2001; 2001WO-EP02882.
XX
PR 14-MAR-2000; 2000US-189091P.
XX
PA (GOEK/) GOEKE B.
PA (SCHI/) SCHIRRA J.
XX
PI Goeke B, Schirra J;
XX
DR WPI; 2001-596887/67.
XX
PT Inhibiting antro-duodenal motility, useful to prevent or treat
PT gastrointestinal disorders such as irritable bowel syndrome and
PT non-infectious diarrhoea, comprises administering glucagon-like peptide
PT -
XX
PS Disclosure; Page 8; 43pp; English.
XX
CC The invention relates to a method of inhibiting antro-duodenal motility
CC in a patient, comprising administering a glucagon-like peptide (GLP-1)
CC molecule. The method is used to premedicate or in endoscopic
CC procedures or to treat or prevent non-infectious acute and chronic
CC diarrhoea, post-operative dumping syndrome, irritable bowel syndrome or
CC symptoms associated with narcotics withdrawal. Unlike prior art treatment
CC with glucagon, the invention is not contraindicated in persons with
CC diabetes, does not incur the risks of side effects such as nausea, and is
CC not expensive. The present sequence represents mammalian glucagon-like
CC peptide-1, GLP-1 (7-37), as described in the method of the invention.
XX
SQ Sequence 31 AA;

AAU07374 Length: 31 January 22, 2004 18:02 Type: P Check: 7361 ..

1 HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID AAE09251 standard; peptide; 31 AA.
XX
AC AAE09251;
XX
DT 15-NOV-2001 (first entry)
XX
DE Human glucagon-like peptide-1 related molecule (GLP)-1(7-37)OH.
XX
KW Human; glucagon-like peptide-1 related molecule; GLP; GLP-1(7-37)OH;
KW GLP crystal; manufacturing process; pharmaceutical formulation; therapy;
KW diabetes; obesity.
XX
OS Homo sapiens.
XX
PN US2001014666-A1.
XX
PD 16-AUG-2001.
XX
PF 11-DEC-1998; 98US-0209799.
XX
PR 11-DEC-1998; 98US-0209799.
XX
PA (HERM/) HERMELING R N.
PA (HOFF/) HOFFMANN J A.
PA (NARA/) NARASIMHAN C.
XX
PI Hermeling RN, Hoffmann JA, Narasimhan C;
XX
DR WPI; 2001-529113/58.
XX
PT Glucagon-like peptide-1 crystals for treating diabetes are prepared
PT from mother liquor containing glucagon-like-peptide-1 related molecules
PT dissolved in buffered solution and alcohol -
XX
PS Example 1; Page 2; 17pp; English.
XX
CC The present sequence is a human glucagon-like peptide-1 related molecule
CC (GLP)-1(7-37)OH. The single tetragonal flat rod-shaped or plate-like
CC crystals of a GLP are prepared from a crystallisation solution containing
CC a GLP, a buffering agent, an alcohol or a mono or disaccharide and
CC optionally ammonium sulphate or zinc. The GLP crystals are used in
CC manufacturing process, in pharmaceutical formulations for treating
CC diabetes, obesity or related conditions in mammals.
XX
SQ Sequence 31 AA;

AAE09251 Length: 31 January 22, 2004 18:02 Type: P Check: 7361 ..

1 HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID AAE09266 standard; peptide; 31 AA.
XX
AC AAE09266;
XX
DT 15-NOV-2001 (first entry)
XX
DE Human DPP-IV protected glucagon-like peptide-1 related molecule #2.
XX
KW Human; glucagon-like peptide-1 related molecule; GLP; GLP crystal;
KW manufacturing process; pharmaceutical formulation; therapy; diabetes;
KW obesity; dipeptidyl-peptidase-IV; DPP-IV.
XX
OS Homo sapiens.
OS Synthetic.
XX
PN US2001014666-A1.
XX
PD 16-AUG-2001.
XX
PF 11-DEC-1998; 98US-0209799.
XX
PR 11-DEC-1998; 98US-0209799.

```
XX
PA   (HERM/) HERMELING R N.
PA   (HOFF/) HOFFMANN J A.
PA   (NARA/) NARASIMHAN C.
XX
PI   Hermeling RN,  Hoffmann JA,  Narasimhan C;
XX
DR   WPI; 2001-529113/58.
XX
PT   Glucagon-like peptide-1 crystals for treating diabetes are prepared
PT   from mother liquor containing glucagon-like-peptide-1 related molecules
PT   dissolved in buffered solution and alcohol  -
XX
PS   Claim 5; Page 13; 17pp; English.
XX
CC   The present sequence is a human dipeptidyl-peptidase-IV (DPP-IV)
CC   protected glucagon-like peptide-1 related molecule (GLP). The single
CC   tetragonal flat rod-shaped or plate-like crystals of a GLP are prepared
CC   from a crystallisation solution containing a GLP, a buffering agent, an
CC   alcohol or a mono or disaccharide and optionally ammonium sulphate or
CC   zinc. The GLP crystals are used in manufacturing process, in
CC   pharmaceutical formulations for treating diabetes, obesity or related
CC   conditions in mammals.
XX
SQ   Sequence   31 AA;

 AAE09266  Length: 31  January 22, 2004 18:02  Type: P  Check: 7373  ..

       1  HGEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID   AAE09267 standard; peptide; 31 AA.
XX
AC   AAE09267;
XX
DT   15-NOV-2001  (first entry)
XX
DE   Human glucagon-like peptide-1 related molecule (GLP)-1 derivative #13.
XX
KW   Human; glucagon-like peptide-1 related molecule; GLP; GLP crystal;
KW   manufacturing process; pharmaceutical formulation; therapy; diabetes;
KW   obesity.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
PN   US2001014666-A1.
XX
PD   16-AUG-2001.
XX
PF   11-DEC-1998;   98US-0209799.
XX
PR   11-DEC-1998;   98US-0209799.
XX
PA   (HERM/) HERMELING R N.
PA   (HOFF/) HOFFMANN J A.
PA   (NARA/) NARASIMHAN C.
XX
PI   Hermeling RN,  Hoffmann JA,  Narasimhan C;
XX
DR   WPI; 2001-529113/58.
XX
PT   Glucagon-like peptide-1 crystals for treating diabetes are prepared
PT   from mother liquor containing glucagon-like-peptide-1 related molecules
PT   dissolved in buffered solution and alcohol  -
XX
PS   Disclosure; Page 13; 17pp; English.
XX
CC   The present sequence is a human glucagon-like peptide-1 related molecule
CC   (GLP)-1 derivative. The single tetragonal flat rod-shaped or plate-like
CC   crystals of a GLP are prepared from a crystallisation solution containing
CC   a GLP, a buffering agent, an alcohol or a mono or disaccharide and
CC   optionally ammonium sulphate or zinc. The GLP crystals are used in
CC   manufacturing process, in pharmaceutical formulations for treating
CC   diabetes, obesity or related conditions in mammals.
XX
SQ   Sequence   31 AA;

 AAE09267  Length: 31  January 22, 2004 18:02  Type: P  Check: 7403  ..

       1  HVEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID   AAE09278 standard; peptide; 31 AA.
XX
AC   AAE09278;
XX
DT   15-NOV-2001  (first entry)
XX
DE   Human glucagon-like peptide-1 related molecule (GLP)-1 derivative #23.
XX
KW   Human; glucagon-like peptide-1 related molecule; GLP; GLP crystal;
KW   manufacturing process; pharmaceutical formulation; therapy; diabetes;
KW   obesity.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
PN   US2001014666-A1.
XX
PD   16-AUG-2001.
XX
PF   11-DEC-1998;   98US-0209799.
XX
PR   11-DEC-1998;   98US-0209799.
XX
PA   (HERM/) HERMELING R N.
PA   (HOFF/) HOFFMANN J A.
PA   (NARA/) NARASIMHAN C.
XX
PI   Hermeling RN,  Hoffmann JA,  Narasimhan C;
XX
DR   WPI; 2001-529113/58.
XX
PT   Glucagon-like peptide-1 crystals for treating diabetes are prepared
PT   from mother liquor containing glucagon-like-peptide-1 related molecules
PT   dissolved in buffered solution and alcohol  -
XX
PS   Disclosure; Page 15; 17pp; English.
XX
CC   The present sequence is a human glucagon-like peptide-1 related molecule
CC   (GLP)-1 derivative. The single tetragonal flat rod-shaped or plate-like
CC   crystals of a GLP are prepared from a crystallisation solution containing
CC   a GLP, a buffering agent, an alcohol or a mono or disaccharide and
CC   optionally ammonium sulphate or zinc. The GLP crystals are used in
CC   manufacturing process, in pharmaceutical formulations for treating
CC   diabetes, obesity or related conditions in mammals.
XX
SQ   Sequence   31 AA;

 AAE09278  Length: 31  January 22, 2004 18:02  Type: P  Check: 7553  ..

       1  HGEGTFTSDV SSYLQGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID   AAG63268 standard; protein; 31 AA.
XX
AC   AAG63268;
XX
DT   01-OCT-2001  (first entry)
XX
DE   Amino acid sequence of an insoluble glucagon-like peptide 1 (GLP-1).
XX
KW   Glucagon-like peptide 1; GLP-1; soluble GLP-1.
XX
OS   Homo sapiens.
```

```
XX
PN   WO200155213-A2.
XX
PD   02-AUG-2001.
XX
PF   16-JAN-2001; 2001WO-US00010.
XX
PR   27-JAN-2000; 2000US-0178438.
PR   09-AUG-2000; 2000US-0224058.
XX
PA   (ELIL ) LILLY & CO ELI.
XX
PI   Prouty WFJ,  Rinella JVJ;
XX
DR   WPI; 2001-476192/51.
XX
PT   Preparing a Glucagon-like peptide 1 compound soluble in aqueous
PT   solution at pH 7.4, comprises dissolving the insoluble form in aqueous
PT   base or acid and neutralizing the solution  -
XX
PS   Claim 4; Page 36; 49pp; English.
XX
CC   The present sequence represents an insoluble glucagon-like peptide 1
CC   (GLP-1). The specification describes a method for preparing a GLP-1
CC   compound that is soluble in aqueous form at pH 7.4 from a GLP-1
CC   compound that is insoluble in aqueous form at pH 7.4. The method
CC   comprises dissolving the insoluble compound in aqueous base or acid;
CC   neutralizing the GLP-1 solution to a pH at which no amino acid
CC   racemisation of the GLP-1 compound occurs; and isolating GLP-1 from
CC   the neutralized solution. The method is used to prepare a soluble form
CC   of a GLP-1 compound. The soluble form of GLP-1 is physiologically active.
XX
SQ   Sequence   31 AA;

 AAG63268  Length: 31  January 22, 2004 18:02  Type: P  Check: 7361  ..

       1  HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID   AAG63272 standard; protein; 31 AA.
XX
AC   AAG63272;
XX
DT   01-OCT-2001  (first entry)
XX
DE   Glucagon-like peptide 1 (GLP-1) analogue Val8-GLP-1(7-37).
XX
KW   Glucagon-like peptide 1; GLP-1; soluble GLP-1.
XX
OS   Synthetic.
XX
PN   WO200155213-A2.
XX
PD   02-AUG-2001.
XX
PF   16-JAN-2001; 2001WO-US00010.
XX
PR   27-JAN-2000; 2000US-0178438.
PR   09-AUG-2000; 2000US-0224058.
XX
PA   (ELIL ) LILLY & CO ELI.
XX
PI   Prouty WFJ,  Rinella JVJ;
XX
DR   WPI; 2001-476192/51.
XX
PT   Preparing a Glucagon-like peptide 1 compound soluble in aqueous
PT   solution at pH 7.4, comprises dissolving the insoluble form in aqueous
PT   base or acid and neutralizing the solution  -
XX
PS   Example 1; Page 18; 49pp; English.
XX
CC   The present sequence represents a glucagon-like peptide 1 (GLP-1)
CC   analogue. The specification describes a method for preparing a GLP-1
CC   compound that is soluble in aqueous form at pH 7.4 from a GLP-1
CC   compound that is insoluble in aqueous form at pH 7.4. The method
CC   comprises dissolving the insoluble compound in aqueous base or acid;
CC   neutralizing the GLP-1 solution to a pH at which no amino acid
CC   racemisation of the GLP-1 compound occurs; and isolating GLP-1 from
CC   the neutralized solution. The method is used to prepare a soluble form
CC   of a GLP-1 compound. The soluble form of GLP-1 is physiologically active.
XX
SQ   Sequence   31 AA;

 AAG63272  Length: 31  January 22, 2004 18:02  Type: P  Check: 7403  ..

       1  HVEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID   AAG63280 standard; protein; 31 AA.
XX
AC   AAG63280;
XX
DT   01-OCT-2001  (first entry)
XX
DE   An insoluble glucagon-like peptide 1 (GLP-1) compound.
XX
KW   Glucagon-like peptide 1; GLP-1; soluble GLP-1.
XX
OS   Synthetic.
XX
PN   WO200155213-A2.
XX
PD   02-AUG-2001.
XX
PF   16-JAN-2001; 2001WO-US00010.
XX
PR   27-JAN-2000; 2000US-0178438.
PR   09-AUG-2000; 2000US-0224058.
XX
PA   (ELIL ) LILLY & CO ELI.
XX
PI   Prouty WFJ,  Rinella JVJ;
XX
DR   WPI; 2001-476192/51.
XX
PT   Preparing a Glucagon-like peptide 1 compound soluble in aqueous
PT   solution at pH 7.4, comprises dissolving the insoluble form in aqueous
PT   base or acid and neutralizing the solution  -
XX
PS   Claim 4; Page 41; 49pp; English.
XX
CC   The present sequence represents an insoluble glucagon-like peptide 1
CC   (GLP-1). The specification describes a method for preparing a GLP-1
CC   compound that is soluble in aqueous form at pH 7.4 from a GLP-1
CC   compound that is insoluble in aqueous form at pH 7.4. The method
CC   comprises dissolving the insoluble compound in aqueous base or acid;
CC   neutralizing the GLP-1 solution to a pH at which no amino acid
CC   racemisation of the GLP-1 compound occurs; and isolating GLP-1 from
CC   the neutralized solution. The method is used to prepare a soluble form
CC   of a GLP-1 compound. The soluble form of GLP-1 is physiologically active.
XX
SQ   Sequence   31 AA;

 AAG63280  Length: 31  January 22, 2004 18:02  Type: P  Check: 7373  ..

       1  HGEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID   AAG63282 standard; protein; 31 AA.
XX
AC   AAG63282;
XX
DT   01-OCT-2001  (first entry)
XX
DE   An insoluble glucagon-like peptide 1 (GLP-1) compound.
```

```
XX
KW   Glucagon-like peptide 1; GLP-1; soluble GLP-1.
XX
OS   Synthetic.
XX
PN   WO200155213-A2.
XX
PD   02-AUG-2001.
XX
PF   16-JAN-2001; 2001WO-US00010.
XX
PR   27-JAN-2000; 2000US-0178438.
PR   09-AUG-2000; 2000US-0224058.
XX
PA   (ELIL ) LILLY & CO ELI.
XX
PI   Prouty WFJ,  Rinella JVJ;
XX
DR   WPI; 2001-476192/51.
XX
PT   Preparing a Glucagon-like peptide 1 compound soluble in aqueous
PT   solution at pH 7.4, comprises dissolving the insoluble form in aqueous
PT   base or acid and neutralizing the solution  -
XX
PS   Claim 4; Page 42; 49pp; English.
XX
CC   The present sequence represents an insoluble glucagon-like peptide 1
CC   (GLP-1). The specification describes a method for preparing a GLP-1
CC   compound that is soluble in aqueous form at pH 7.4 from a GLP-1
CC   compound that is insoluble in aqueous form at pH 7.4. The method
CC   comprises dissolving the insoluble compound in aqueous base or acid;
CC   neutralizing the GLP-1 solution to a pH at which no amino acid
CC   racemisation of the GLP-1 compound occurs; and isolating GLP-1 from
CC   the neutralized solution. The method is used to prepare a soluble form
CC   of a GLP-1 compound. The soluble form of GLP-1 is physiologically active.
XX
SQ   Sequence   31 AA;

 AAG63282  Length: 31  January 22, 2004 18:02  Type: P  Check: 7403  ..

       1  HVEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID   AAG63302 standard; protein; 31 AA.
XX
AC   AAG63302;
XX
DT   01-OCT-2001  (first entry)
XX
DE   An insoluble glucagon-like peptide 1 (GLP-1) compound.
XX
KW   Glucagon-like peptide 1; GLP-1; soluble GLP-1.
XX
OS   Synthetic.
XX
PN   WO200155213-A2.
XX
PD   02-AUG-2001.
XX
PF   16-JAN-2001; 2001WO-US00010.
XX
PR   27-JAN-2000; 2000US-0178438.
PR   09-AUG-2000; 2000US-0224058.
XX
PA   (ELIL ) LILLY & CO ELI.
XX
PI   Prouty WFJ,  Rinella JVJ;
XX
DR   WPI; 2001-476192/51.
XX
PT   Preparing a Glucagon-like peptide 1 compound soluble in aqueous
PT   solution at pH 7.4, comprises dissolving the insoluble form in aqueous
PT   base or acid and neutralizing the solution  -
XX
PS   Claim 4; Page 49; 49pp; English.
XX
CC   The present sequence represents an insoluble glucagon-like peptide 1
CC   (GLP-1). The specification describes a method for preparing a GLP-1
CC   compound that is soluble in aqueous form at pH 7.4 from a GLP-1
CC   compound that is insoluble in aqueous form at pH 7.4. The method
CC   comprises dissolving the insoluble compound in aqueous base or acid;
CC   neutralizing the GLP-1 solution to a pH at which no amino acid
CC   racemisation of the GLP-1 compound occurs; and isolating GLP-1 from
CC   the neutralized solution. The method is used to prepare a soluble form
CC   of a GLP-1 compound. The soluble form of GLP-1 is physiologically active.
XX
SQ   Sequence   31 AA;

 AAG63302  Length: 31  January 22, 2004 18:02  Type: P  Check: 7553  ..

       1  HGEGTFTSDV SSYLQGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID   AAB82335 standard; Peptide; 31 AA.
XX
AC   AAB82335;
XX
DT   23-JUL-2001  (first entry)
XX
DE   Glucagon-like peptide 1 (7-37).
XX
KW   Somatostatin; glucagon-like peptide 1; GLP-1; antidiabetic;
KW   drug delivery; diabetes; gene therapy.
XX
OS   Homo sapiens.
XX
PN   WO200136643-A1.
XX
PD   25-MAY-2001.
XX
PF   17-NOV-2000; 2000WO-US31634.
XX
PR   19-NOV-1999;   99US-0166508.
XX
PA   (TRAN-) TRANSKARYOTIC THERAPIES INC.
XX
PI   Treco DA,  Concino MF,  Duguay SJ;
XX
DR   WPI; 2001-355636/37.
XX
PT   New nucleic acid constructs useful for transforming cells useful as a
PT   drug delivery vehicle -
XX
PS   Example 3; Fig 4; 89pp; English.
XX
CC   The present sequence is that of amino acid residues 7-37 of human
CC   glucagon-like peptide 1 (GLP-1).  The peptide is secreted by
CC   human fibroblasts transfected with pXIT-39 (see AAF30989).  pXIT-39
CC   is an example of novel nucleic acid constructs of the invention,
CC   that have been designed for the expression of small peptides,
CC   especially an antidiabetic peptide such as GLP-1(7-37) and
CC   GLP-1(7-36).  They comprise: a nucleic acid sequence encoding a
CC   signal peptide; a nucleic acid sequence encoding the pro-region of
CC   somatostatin, its functional fragment or analogue; and a nucleic
CC   acid encoding the small peptide.  The construct may also comprise a
CC   cleavage site between the pro-region and the sequence encoding the
CC   small peptide.  Claimed methods of treating a subject having
CC   diabetes involve administering the nucleic acid construct or a cell
CC   capable of expressing the small peptide.  Transfected primary or
CC   secondary cells or cell strains have wide applicability as vehicles
CC   or delivery systems for therapeutic proteins such as GLP-1.  By
CC   controlling the number of cells introduced into an individual, one
CC   can control the amount of the protein delivered to the body.  In
CC   some cases, it is possible to remove the transfected cells if there
CC   is no longer a need for the product.
XX
```

```
SQ   Sequence   31 AA;

 AAB82335  Length: 31  January 22, 2004 18:02  Type: P  Check: 7361  ..

      1  HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID   AAB91169 standard; Peptide; 37 AA.
XX
AC   AAB91169;
XX
DT   22-JUN-2001  (first entry)
XX
DE   Pancreatic hormone glucagon peptide SEQ ID NO:343.
XX
KW   Protection; endogenous therapeutic peptide; peptidase; conjugation;
KW   blood component; modification; succinimidyl; maleimido group; amino;
KW   hydroxyl; thiol; hormone; growth factor; neurotransmitter.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
PN   WO200069900-A2.
XX
PD   23-NOV-2000.
XX
PF   17-MAY-2000; 2000WO-US13576.
XX
PR   17-MAY-1999;   99US-0134406.
PR   10-SEP-1999;   99US-0153406.
PR   15-OCT-1999;   99US-0159783.
XX
PA   (CONJ-) CONJUCHEM INC.
XX
PI   Bridon DP,  Ezrin AM,  Milner PG,  Holmes DL,  Thibaudeau K;
XX
DR   WPI; 2001-112059/12.
XX
PT   Modifying and attaching therapeutic peptides to albumin prevents
PT   peptidase degradation, useful for increasing length of in vivo activity
PT   -
XX
PS   Disclosure; Page 307; 733pp; English.
XX
CC   The present invention describes a modified therapeutic peptide (I)
CC   comprising a therapeutically active amino acid region (III) and a
CC   reactive group (II) (e.g. succinimidyl and maleimido groups) attached to
CC   a less therapeutically active amino acid region (IV), which covalently
CC   bonds with amino/hydroxyl/thiol groups on blood components to form a
CC   peptidase stabilised therapeutic peptide composed of 3-50 amino acids.
CC   (I) are useful for modifying therapeutic peptides e.g. hormones, growth
CC   factors and neurotransmitters, to protect them from peptidase activity
CC   in vivo for the treatment of various disorders. Endogenous therapeutic
CC   peptides are not suitable as drug candidates as they require frequent
CC   administration due to rapid degradation by peptidases in the body.
CC   Modifying and attaching therapeutic peptides to albumin prevents or
CC   reduces the action of peptidases to increase length of activity (half
CC   life) and specificity as bonding to large molecules decreases
CC   intracellular uptake and interference with physiological processes.
CC   AAB90829 to AAB92441 represent peptides which can be used in the
CC   exemplification of the present invention.
XX
SQ   Sequence   37 AA;

 AAB91169  Length: 37  January 22, 2004 18:02  Type: P  Check: 2897  ..

      1  HDEFERHAEG TFTSDVSSYL EGQAAKEFIA WLVKGRG

!!AA_SEQUENCE 1.0
ID   AAB30702 standard; Protein; 378 AA.
XX
AC   AAB30702;
XX
DT   02-APR-2001  (first entry)
XX
DE   A Bacillus pectate lyase and human GLP-1 hormone fusion protein.
XX
KW   Pectate lyase; pectinase; alpha-1,4-glycosidic linkage; pectic acid;
KW   polygalacturonic acid; GLP-1.
XX
OS   Synthetic.
OS   Bacillus licheniformis.
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1. .29
FT                   /note= "signal peptide"
FT   Protein         30. .343
FT                   /note= "pectate lyase"
FT   Cleavage-site   346. .347
FT                   /note= "Kex 2 endoprotease processing site"
FT   Protein         348. .378
FT                   /note= "GLP-1"
XX
PN   WO200075344-A1.
XX
PD   14-DEC-2000.
XX
PF   31-MAY-2000; 2000WO-DK00296.
XX
PR   02-JUN-1999;   99DK-0000780.
PR   11-JUN-1999;   99US-0138692.
XX
PA   (NOVO ) NOVO NORDISK AS.
XX
PI   Rasmussen MD,  Bjoernvad ME,  Diers I;
XX
DR   WPI; 2001-071079/08.
DR   N-PSDB; AAC86599.
XX
PT   Bacillus cells having a DNA sequence coding for a pectate lyase, a
PT   proteolytic cleavage target site, or a polypeptide of exogenous origin
PT   fused sequentially into one open reading frame, for producing fusion
PT   proteins in higher yields -
XX
PS   Claim 19; Page 75-77; 94pp; English.
XX
CC   The present sequence encodes a fusion protein of a Bacillus pectate
CC   lyase polypeptide and a human GLP-1 hormone polypeptide. Pectate
CC   lyase is a pectinase which catalyses the random cleavage of
CC   alpha-1,4-glycosidic linkages in pectic acid (polygalacturonic acid).
CC   The fusion polypeptide is expressed using the cells of the invention.
CC   The specification describes a cell for improved production of a fusion
CC   protein comprising a native pectate lyase fused to an exogenous
CC   polypeptide. The cell is preferably a gram positive cell. The cell is
CC   useful for the production of higher yields of fusion proteins or
CC   polypeptides, which have been difficult to obtain, such as active human
CC   antibodies.
XX
SQ   Sequence   378 AA;

AAB30702  Length: 378  January 22, 2004 18:02  Type: P  Check: 1397  ..

      1  MKQQKRLYAR LLTLLFALIF LLPHSAAAAA SALNSGKVNP LADPSLKGFA

     51  ALNGGTTGGE GGQTVTVTTG DQLIAALKNK NANTPLKIYV NGTITTSNTS

    101  ASKIDVKDVS NVSIVGSGTK GELKGIGIKI WRANNIIIRN LKIHEVASGD

    151  KDAIGIEGPS KNIWVDHNEL YHSLNVDKDY YDGLFDVKRD AEYITFSWNY

    201  VHDGWKSMLM GSSDSDNYNR TITFHHNWFE NLNSRVPSFR FGEGHIYNNY

    251  FNKIIDSGIN SRMGARIRIE NNLFENAKDP IVSWYSSSPG YWHVSNNKFV

    301  NSRGSMPTTS TTTYNPPYSY SLDNVDNVKS IVKQNAGVGK INPASKRHAE
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     351  GTFTSDVSSY LEGQAAKEFI AWLVKGRG

!!AA_SEQUENCE 1.0
ID   AAB30703 standard; Protein; 386 AA.
XX
AC   AAB30703;
XX
DT   02-APR-2001  (first entry)
XX
DE   A Bacillus pectate lyase and human GLP-1 hormone fusion protein.
XX
KW   Pectate lyase; pectinase; alpha-1,4-glycosidic linkage; pectic acid;
KW   polygalacturonic acid; GLP-1.
XX
OS   Synthetic.
OS   Bacillus licheniformis.
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1. .29
FT                   /note= "signal peptide"
FT   Protein         30. .343
FT                   /note= "pectate lyase"
FT   Peptide         346. .353
FT                   /note= "PEPTPEPT linker"
FT   Cleavage-site   354. .355
FT                   /note= "Kex 2 endoprotease processing site"
FT   Protein         356. .386
FT                   /note= "GLP-1"
XX
PN   WO200075344-A1.
XX
PD   14-DEC-2000.
XX
PF   31-MAY-2000; 2000WO-DK00296.
XX
PR   02-JUN-1999;   99DK-0000780.
PR   11-JUN-1999;   99US-0138692.
XX
PA   (NOVO ) NOVO NORDISK AS.
XX
PI   Rasmussen MD,  Bjoernvad ME,  Diers I;
XX
DR   WPI; 2001-071079/08.
DR   N-PSDB; AAC86600.
XX
PT   Bacillus cells having a DNA sequence coding for a pectate lyase, a
PT   proteolytic cleavage target site, or a polypeptide of exogenous origin
PT   fused sequentially into one open reading frame, for producing fusion
PT   proteins in higher yields -
XX
PS   Claim 19; Page 79-81; 94pp; English.
XX
CC   The present sequence encodes a fusion protein of a Bacillus pectate
CC   lyase polypeptide and a human GLP-1 hormone polypeptide. Pectate
CC   lyase is a pectinase which catalyses the random cleavage of
CC   alpha-1,4-glycosidic linkages in pectic acid (polygalacturonic acid).
CC   The fusion polypeptide is expressed using the cells of the invention.
CC   The specification describes a cell for improved production of a fusion
CC   protein comprising a native pectate lyase fused to an exogenous
CC   polypeptide. The cell is preferably a gram positive cell. The cell is
CC   useful for the production of higher yields of fusion proteins or
CC   polypeptides, which have been difficult to obtain, such as active human
CC   antibodies.
XX
SQ   Sequence   386 AA;

AAB30703  Length: 386  January 22, 2004 18:02  Type: P  Check: 6043  ..

       1  MKQQKRLYAR LLTLLFALIF LLPHSAAAAA SALNSGKVNP LADFSLKGFA

      51  ALNGGTTGGE GGQTVTVTTG DQLIAALKNK NANTPLKIYV NGTITTSNTS

     101  ASKIDVKDVS NVSIVGSGTK GELKGIGIKI WRANNIIIRN LKIHEVASGD

     151  KDAIGIEGPS KNIWVDHNEL YHSLNVDKDY YDGLFDVKRD AEYITFSWNY

     201  VHDGWKSMLM GSSDSDNYNR TITFHHNWFE NLNSRVPSFR FGEGHIYNNY

     251  FNKIIDSGIN SRMGARIRIE NNLFENAKDP IVSWYSSSPG YWHVSNNKFV

     301  NSRGSMPTTS TTTYNPPYSY SLDNVDNVKS IVKQNAGVGK INPASPEPTP

     351  EPTKRHAEGT FTSDVSSYLE GQAAKEFIAW LVKGRG

!!AA_SEQUENCE 1.0
ID   AAB49694 standard; peptide; 31 AA.
XX
AC   AAB49694;
XX
DT   04-APR-2001  (first entry)
XX
DE   Glucagon-like peptide 1 (GLP-1) amino acid sequence.
XX
KW   Glucagon-like peptide I; 1-37; anti-diabetic; hypoglycaemic;
KW   insulin expression stimulator; maturity onset diabetes mellitus;
KW   hyperglycaemia.
XX
OS   Unidentified.
XX
PN   US6162907-A.
XX
PD   19-DEC-2000.
XX
PF   05-JUN-1998;   98US-0090949.
XX
PR   26-JAN-1988;   88US-0148517.
PR   05-SEP-1991;   91US-0756215.
PR   23-NOV-1993;   93US-0156800.
PR   20-NOV-1996;   96US-0749762.
PR   05-MAY-1986;   86US-0859928.
PR   01-JUN-1990;   90US-0532111.
XX
PA   (GEHO ) GEN HOSPITAL CORP.
XX
PI   Habener JF;
XX
DR   WPI; 2001-090410/10.
XX
PT   New DNA molecule encoding a fragment(7-37) of glucagon-like peptide 1
PT   which has insulinotropic activity, and differs from the native 37 amino
PT   acid residue peptide(7-37) of GLP-1 useful for treating type II
PT   diabetes mellitus -
XX
PS   Claim 1; Column 32; 37pp; English.
XX
CC   This invention relates to DNA encoding a fragment of glucagon-like
CC   peptide I (1-37) represented by peptide AAB49694, which does not encode
CC   the native GLP-1 (1-37) peptide represented in AAB49695. The peptide has
CC   anti-diabetic and hypoglycaemic activity, and works as a insulin
CC   expression stimulator. The insulinotropic hormone encoded by the DNA
CC   sequence of the invention is useful in the study of the pathogenesis of
CC   maturity onset diabetes mellitus and in the therapy and treatment of
CC   diabetes mellitus and hyperglycaemia.
XX
SQ   Sequence   31 AA;

 AAB49694  Length: 31  January 22, 2004 18:02  Type: P  Check: 7361  ..

       1  HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID   AAB49695 standard; peptide; 37 AA.
XX
AC   AAB49695;
```

```
XX
DT   04-APR-2001  (first entry)
XX
DE   Glucagon-like peptide 1 (GLP-1) native amino acid sequence.
XX
KW   Glucagon-like peptide I; 1-37; anti-diabetic; hypoglycaemic;
KW   insulin expression stimulator; maturity onset diabetes mellitus;
KW   hyperglycaemia.
XX
OS   Unidentified.
XX
PN   US6162907-A.
XX
PD   19-DEC-2000.
XX
PF   05-JUN-1998;   98US-0090949.
XX
PR   26-JAN-1988;   88US-0148517.
PR   05-SEP-1991;   91US-0756215.
PR   23-NOV-1993;   93US-0156800.
PR   20-NOV-1996;   96US-0749762.
PR   05-MAY-1986;   86US-0859928.
PR   01-JUN-1990;   90US-0532111.
XX
PA   (GEHO ) GEN HOSPITAL CORP.
XX
PI   Habener JF;
XX
DR   WPI; 2001-090410/10.
XX
PT   New DNA molecule encoding a fragment(7-37) of glucagon-like peptide 1
PT   which has insulinotropic activity, and differs from the native 37 amino
PT   acid residue peptide(7-37) of GLP-1 useful for treating type II
PT   diabetes mellitus -
XX
PS   Disclosure; Column 32; 37pp; English.
XX
CC   This invention relates to DNA encoding a fragment of glucagon-like
CC   peptide I (1-37) represented by peptide AAB49694, which does not encode
CC   the native GLP-1 (1-37) peptide represented in AAB49695. The peptide has
CC   anti-diabetic and hypoglycaemic activity, and works as a insulin
CC   expression stimulator. The insulinotropic hormone encoded by the DNA
CC   sequence of the invention is useful in the study of the pathogenesis of
CC   maturity onset diabetes mellitus and in the therapy and treatment of
CC   diabetes mellitus and hyperglycaemia. The present sequence represents the
CC   native GLP-1 (1-37) peptide which is specifically not claimed.
XX
SQ   Sequence   37 AA;

 AAB49695  Length: 37  January 22, 2004 18:02  Type: P  Check: 2897  ..

       1  HDEFERHAEG TFTSDVSSYL EGQAAKEFIA WLVKGRG

!!AA_SEQUENCE 1.0
ID   AAB60246 standard; peptide; 37 AA.
XX
AC   AAB60246;
XX
DT   28-MAR-2001  (first entry)
XX
DE   Glucagon-like peptide-1, GLP-1 (1-37).
XX
KW   Glucagon-like peptide-1; GLP-1 (1-37); type II diabetes;
KW   non-insulin dependent diabetes mellitus; NIDDM; beta-cell function;
KW   secretory capacity; impaired glucose tolerance; IGT;
KW   beta-cell stimulatory test; diagnostic test; insulinotropic.
XX
OS   Homo sapiens.
XX
PN   WO200077039-A2.
XX
PD   21-DEC-2000.
XX
PF   14-JUN-2000; 2000WO-US16428.
XX
PR   15-JUN-1999;  99US-0333415.
XX
PA   (BION-) BIONEBRASKA INC.
XX
PI   Holst JJ,  Vilsboll T;
XX
DR   WPI; 2001-102518/11.
XX
PT   Evaluating beta-cell secretory capacity and responsiveness to glucose,
PT   useful for diagnosing impaired glucose tolerance and diabetes,
PT   comprises employing glucagon-like-peptide-1 as a diagnostic test to
PT   determine beta-cell function -
XX
PS   Disclosure; Page 11; 42pp; English.
XX
CC   The invention relates to a new method for evaluating beta-cell secretory
CC   capacity in an individual, or responsiveness of a beta-cell to glucose,
CC   comprising the administration of glucose and glucagon-like peptide-1
CC   (GLP-1) or its biologically active analogues. The response in the
CC   individual is then measured against the standard response of a healthy
CC   individual to determine if the individual has impaired beta-cell
CC   function. The method is useful for detecting impaired beta-cell function
CC   in an individual, and is particularly useful for diagnosing impaired
CC   glucose tolerance (IGT) and non-insulin-dependent (type II) diabetes.
CC   The method is a rapid test of beta-cell function, which is a marker for
CC   impaired glucose tolerance. Unlike prior methods, the method is reliable
CC   and without significant adverse side effects and/or patient pain and
CC   discomfort. The method also provides information about insulin secretory
CC   capacity, and is easy and reproducible. The present sequence represents
CC   a GLP-1 related peptide referred to in the disclosure of the invention.
XX
SQ   Sequence   37 AA;

 AAB60246  Length: 37  January 22, 2004 18:02  Type: P  Check: 2897  ..

       1  HDEFERHAEG TFTSDVSSYL EGQAAKEFIA WLVKGRG

!!AA_SEQUENCE 1.0
ID   AAB60248 standard; peptide; 31 AA.
XX
AC   AAB60248;
XX
DT   28-MAR-2001  (first entry)
XX
DE   Glucagon-like peptide-1, GLP-1 (7-37).
XX
KW   Glucagon-like peptide-1; GLP-1 (7-37); type II diabetes;
KW   non-insulin dependent diabetes mellitus; NIDDM; beta-cell function;
KW   secretory capacity; impaired glucose tolerance; IGT;
KW   beta-cell stimulatory test; diagnostic test; insulinotropic.
XX
OS   Homo sapiens.
XX
PN   WO200077039-A2.
XX
PD   21-DEC-2000.
XX
PF   14-JUN-2000; 2000WO-US16428.
XX
PR   15-JUN-1999;  99US-0333415.
XX
PA   (BION-) BIONEBRASKA INC.
XX
PI   Holst JJ,  Vilsboll T;
XX
DR   WPI; 2001-102518/11.
XX
PT   Evaluating beta-cell secretory capacity and responsiveness to glucose,
PT   useful for diagnosing impaired glucose tolerance and diabetes,
PT   comprises employing glucagon-like-peptide-1 as a diagnostic test to
PT   determine beta-cell function -
```

XX
PS Claim 4; Page 11; 42pp; English.
XX
CC The invention relates to a new method for evaluating beta-cell secretory
CC capacity in an individual, or responsiveness of a beta-cell to glucose,
CC comprising the administration of glucose and glucagon-like peptide-1
CC (GLP-1) or its biologically active analogues. The response in the
CC individual is then measured against the standard response of a healthy
CC individual to determine if the individual has impaired beta-cell
CC function. The method is useful for detecting impaired beta-cell function
CC in an individual, and is particularly useful for diagnosing impaired
CC glucose tolerance (IGT) and non-insulin-dependent (type II) diabetes.
CC The method is a rapid test of beta-cell function, which is a marker for
CC impaired glucose tolerance. Unlike prior methods, the method is reliable
CC and without significant adverse side effects and/or patient pain and
CC discomfort. The method also provides information about insulin secretory
CC capacity, and is easy and reproducible. The present sequence represents
CC a GLP-1 related peptide specifically claimed for use in the method
CC of the invention.
XX
SQ Sequence 31 AA;

AAB60248 Length: 31 January 22, 2004 18:02 Type: P Check: 7361 ..

1 HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID AAB48790 standard; peptide; 37 AA.
XX
AC AAB48790;
XX
DT 09-MAR-2001 (first entry)
XX
DE Glucagon-like peptide 1 (GLP-1), SEQ ID NO:1.
XX
KW Insulinotropic peptide; insulin production; GLP-1 derivative;
KW glucagon-like peptide 1; exendin derivative; reactive group;
KW peptidase stabilisation; blood protein; conjugation; type II diabetes;
KW insulin resistance; nervous system disorder; sedative; anxiolytic;
KW antidiabetic; neuroprotective; tranquiliser; anticonvulsant.
XX
OS Unidentified.
XX
PN WO200069911-A1.
XX
PD 23-NOV-2000.
XX
PF 17-MAY-2000; 2000WO-US13563.
XX
PR 17-MAY-1999; 99US-0134406.
PR 15-OCT-1999; 99US-0159783.
XX
PA (CONJ-) CONJUCHEM INC.
XX
PI Bridon DP, L'Archeveque B, Ezrin AM, Holmes DL, Leblanc A;
PI St Pierre S;
XX
DR WPI; 2001-025008/03.
XX
PT Novel modified insulinotropic peptides for treating diabetes, nervous
PT system disorders and for post surgery treatment, has reactive groups
PT which react with amino, hydroxy or thiol groups on blood components -
XX
PS Disclosure; Page 85; 96pp; English.
XX
CC The invention relates to modified insulinotropic peptides (ITPs), or
CC derivatives thereof which comprise a reactive group which reacts with
CC amino groups, hydroxyl groups or thiol groups on blood components (e.g.,
CC serum albumin) to form a stable covalent bond. The insulinotropic
CC peptides of the invention are derivatives of glucagon-like peptide 1
CC (GLP-1) or exendin and contain a reactive group such as a maleimido
CC group or a succinimidyl group. The peptides of the invention act by
CC stimulating the synthesis or expression of insulin. A composition
CC comprising a peptide of the invention is useful for treating diabetes,
CC paticularly type II (maturity onset) diabetes. It is also useful as a
CC sedative; for the treatment of nervous system disorders including
CC anxiety, psychosis, seizures, panic attacks, hysteria and sleep
CC disorders; to induce an anxiolytic effect on the cehtral nervous system
CC (CNS); to activate the CNS for the treatment of disprders such as
CC depression, memory loss and narcolepsy; and as a treatment for
CC insulin resistance, particularly that which occurs after certain types
CC of surgery. The conjugation of a peptide of the invention to a
CC blood component via the reactive group provides increased stability in
CC the presence of peptidases. The peptides of the invention therefore
CC have a longer in vivo. half-life as they are less susceptible to
CC proteolytic degradation. The present sequence represents an
CC insulinotropic peptide referred to in the disclosure of the invention.
XX
SQ Sequence 37 AA;

AAB48790 Length: 37 January 22, 2004 18:02 Type: P Check: 2897 ..

1 HDEFERHAEG TFTSDVSSYL EGQAAKEFIA WLVKGRG

!!AA_SEQUENCE 1.0
ID AAB48791 standard; peptide; 31 AA.
XX
AC AAB48791;
XX
DT 09-MAR-2001 (first entry)
XX
DE Glucagon-like peptide 1 derivative GLP-1(7-37), SEQ ID NO:2.
XX
KW Insulinotropic peptide; insulin production; GLP-1 derivative;
KW glucagon-like peptide 1; exendin derivative; reactive group;
KW peptidase stabilisation; blood protein; conjugation; type II diabetes;
KW insulin resistance; nervous system disorder; sedative; anxiolytic;
KW antidiabetic; neuroprotective; tranquiliser; anticonvulsant.
XX
OS Synthetic.
XX
PN WO200069911-A1.
XX
PD 23-NOV-2000.
XX
PF 17-MAY-2000; 2000WO-US13563.
XX
PR 17-MAY-1999; 99US-0134406.
PR 15-OCT-1999; 99US-0159783.
XX
PA (CONJ-) CONJUCHEM INC.
XX
PI Bridon DP, L'Archeveque B, Ezrin AM, Holmes DL, Leblanc A;
PI St Pierre S;
XX
DR WPI; 2001-025008/03.
XX
PT Novel modified insulinotropic peptides for treating diabetes, nervous
PT system disorders and for post surgery treatment, has reactive groups
PT which react with amino, hydroxy or thiol groups on blood components -
XX
PS Claim 4; Page 86; 96pp; English.
XX
CC The invention relates to modified insulinotropic peptides (ITPs), or
CC derivatives thereof which comprise a reactive group which reacts with
CC amino groups, hydroxyl groups or thiol groups on blood components (e.g.,
CC serum albumin) to form a stable covalent bond. The insulinotropic
CC peptides of the invention are derivatives of glucagon-like peptide 1
CC (GLP-1) or exendin and contain a reactive group such as a maleimido
CC group or a succinimidyl group. The peptides of the invention act by
CC stimulating the synthesis or expression of insulin. A composition
CC comprising a peptide of the invention is useful for treating diabetes,
CC paticularly type II (maturity onset) diabetes. It is also useful as a
CC sedative; for the treatment of nervous system disorders including
CC anxiety, psychosis, seizures, panic attacks, hysteria and sleep
CC disorders; to induce an anxiolytic effect on the central nervous system

CC (CNS); to activate the CNS for the treatment of disorders such as
CC depression, memory loss and narcolepsy; and as a treatment for
CC insulin resistance, particularly that which occurs after certain types
CC of surgery. The conjugation of a peptide of the invention to a
CC blood component via the reactive group provides increased stability in
CC the presence of peptidases. The peptides of the invention therefore
CC have a longer in vivo. half-life as they are less susceptible to
CC proteolytic degradation. The present sequence represents an
CC insulinotropic peptide of the invention.
XX
SQ Sequence 31 AA;

AAB48791 Length: 31 January 22, 2004 18:02 Type: P Check: 7361 ..

1 HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID AAB36413 standard; peptide; 37 AA.
XX
AC AAB36413;
XX
DT 28-FEB-2001 (first entry)
XX
DE Glucagon-like peptide-1 (1-37) SEQ ID NO:1.
XX
KW Glucagon-like peptide-1; GLP-1; GLP-2; vasotropic; cerebroprotective;
KW brain tissue injury; reperfusion; blood flow; ischaemia; acute stroke;
KW metabolic intervention; haemorrhage; tissue damage; medical procedure;
KW surgical; insulin; hyperglycaemia; hypoglycaemia; brain anabolism;
KW euglycaemia.
XX
OS Mammalia.
XX
PN WO200066142-A2.
XX
PD 09-NOV-2000.
XX
PF 01-MAY-2000; 2000WO-US11652.
XX
PR 30-APR-1999; 99US-0303016.
XX
PA (BION-) BIONEBRASKA INC.
XX
PI Coolidge TR, Ehlers MRW;
XX
DR WPI; 2001-015911/02.
XX
PT A method for amelioration of brain tissue injury comprises
PT administering a composition including a compound which binds to a
PT receptor for glucagon-like peptide-1 -
XX
PS Disclosure; Page 7; 19pp; English.
XX
CC The present invention describes a method for the amelioration of brain
CC tissue injury caused by reperfusion of blood flow comprising
CC administering a composition including a compound which binds to a
CC receptor for glucagon-like peptide-1 (GLP-1), in a pharmaceutical
CC carrier. The method is used for amelioration of brain tissue injury
CC caused by reperfusion of blood flow following a period of ischaemia.
CC GLP-1 is used for metabolic intervention to improve the function of
CC ischaemic and reperfused brain cells. It treats patients after an acute
CC stroke or haemorrhage and tissue damage arising from a medical procedure
CC that is a surgical event causing ischaemia of brain tissue or a medical
CC procedure involving a reperfusion event. GLP-1 is an ideal alternative
CC to insulin for the treatment of stroke as it stimulates endogenous
CC insulin secretion in the presence of normo- to hyperglycaemia but not
CC during hypoglycaemia, thus protecting against the development of severe
CC hypoglycaemia. The treatment optimises insulin secretion, increases
CC brain anabolism, enhancing insulin effectiveness by suppressing glucagon
CC and maintains euglycaemia or mild hypoglycaemia with no risk of severe
CC hypoglycaemia. The present sequence represents a GLP-1 peptide which is
CC given in the exemplification of the present invention.
XX
SQ Sequence 37 AA;

AAB36413 Length: 37 January 22, 2004 18:02 Type: P Check: 2897 ..

1 HDEFERHAEG TFTSDVSSYL EGQAAKEFIA WLVKGRG

!!AA_SEQUENCE 1.0
ID AAB36415 standard; peptide; 31 AA.
XX
AC AAB36415;
XX
DT 28-FEB-2001 (first entry)
XX
DE Glucagon-like peptide-1 (7-37) SEQ ID NO:3.
XX
KW Glucagon-like peptide-1; GLP-1; GLP-2; vasotropic; cerebroprotective;
KW brain tissue injury; reperfusion; blood flow; ischaemia; acute stroke;
KW metabolic intervention; haemorrhage; tissue damage; medical procedure;
KW surgical; insulin; hyperglycaemia; hypoglycaemia; brain anabolism;
KW euglycaemia.
XX
OS Mammalia.
XX
PN WO200066142-A2.
XX
PD 09-NOV-2000.
XX
PF 01-MAY-2000; 2000WO-US11652.
XX
PR 30-APR-1999; 99US-0303016.
XX
PA (BION-) BIONEBRASKA INC.
XX
PI Coolidge TR, Ehlers MRW;
XX
DR WPI; 2001-015911/02.
XX
PT A method for amelioration of brain tissue injury comprises
PT administering a composition including a compound which binds to a
PT receptor for glucagon-like peptide-1 -
XX
PS Disclosure; Page 7; 19pp; English.
XX
CC The present invention describes a method for the amelioration of brain
CC tissue injury caused by reperfusion of blood flow comprising
CC administering a composition including a compound which binds to a
CC receptor for glucagon-like peptide-1 (GLP-1), in a pharmaceutical
CC carrier. The method is used for amelioration of brain tissue injury
CC caused by reperfusion of blood flow following a period of ischaemia.
CC GLP-1 is used for metabolic intervention to improve the function of
CC ischaemic and reperfused brain cells. It treats patients after an acute
CC stroke or haemorrhage and tissue damage arising from a medical procedure
CC that is a surgical event causing ischaemia of brain tissue or a medical
CC procedure involving a reperfusion event. GLP-1 is an ideal alternative
CC to insulin for the treatment of stroke as it stimulates endogenous
CC insulin secretion in the presence of normo- to hyperglycaemia but not
CC during hypoglycaemia, thus protecting against the development of severe
CC hypoglycaemia. The treatment optimises insulin secretion, increases
CC brain anabolism, enhancing insulin effectiveness by suppressing glucagon
CC and maintains euglycaemia or mild hypoglycaemia with no risk of severe
CC hypoglycaemia. The present sequence represents a GLP-1 peptide which is
CC given in the exemplification of the present invention.
XX
SQ Sequence 31 AA;

AAB36415 Length: 31 January 22, 2004 18:02 Type: P Check: 7361 ..

1 HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID AAB36426 standard; peptide; 37 AA.
XX
AC AAB36426;

XX
DT 28-FEB-2001 (first entry)
XX
DE Glucagon-like peptide-1 (1-37) SEQ ID NO:1.
XX
KW Glucagon-like peptide-1; GLP-1; GLP-2; metabolic intervention;
KW ischaemia; reperfusion; surgical procedure; cardiac surgical procedure;
KW organ transplant; traumatic limb amputation; limb reattachment;
KW ischaemic reperfusion; gut infarct; myocardial infarct.
XX
OS Mammalia.
XX
PN WO200066138-A2.
XX
PD 09-NOV-2000.
XX
PF 27-APR-2000; 2000WO-US11251.
XX
PR 30-APR-1999; 99US-0302596.
XX
PA (BION-) BIONEBRASKA INC.
XX
PI Coolidge TR, Ehlers MRW;
XX
DR WPI; 2001-040881/05.
XX
PT Metabolic intervention with GLP-1 improves function of ischemic and
PT reperfused tissue -
XX
PS Disclosure; Page 11; 22pp; English.
XX
CC The present invention describes metabolic intervention with GLP-1 which
CC improves the function of ischaemic and reperfused tissue. The method for
CC amelioration of organ tissue caused by reperfusion of blood flow
CC following a period of ischaemia comprises administering a composition
CC including a compound which binds to a receptor for glucagon-like
CC peptide-1 (GLP-1), in a carrier. Also described are: (1) a method of
CC metabolic intervention with GLP-1 to improve the function of ischaemic
CC and reperfused tissue, the method comprising administering a composition
CC comprising GLP-1 in a carrier; and (2) a composition for use in the
CC metabolic intervention with GLP-1 as above. The method is useful after
CC surgical procedures selected from cardiac surgical procedures, organ
CC transplants, traumatic limb amputation and reattachment, a ischaemic
CC reperfusion event concurrent with gut infarct and myocardial infarct
CC and improves the function of ischaemic and reperfused tissues. The
CC method is devoid of side effects associated with current procedures.
CC Antigenic and immune stimulating properties are not adversely affected.
CC The present sequence represents a GLP-1 peptide which is given in the
CC exemplification of the present invention.
XX
SQ Sequence 37 AA;

AAB36426 Length: 37 January 22, 2004 18:02 Type: P Check: 2897 ..

1 HDEFERHAEG TFTSDVSSYL EGQAAKEFIA WLVKGRG

!!AA_SEQUENCE 1.0
ID AAB36428 standard; peptide; 31 AA.
XX
AC AAB36428;
XX
DT 28-FEB-2001 (first entry)
XX
DE Glucagon-like peptide-1 (7-37) SEQ ID NO:3.
XX
KW Glucagon-like peptide-1; GLP-1; GLP-2; metabolic intervention;
KW ischaemia; reperfusion; surgical procedure; cardiac surgical procedure;
KW organ transplant; traumatic limb amputation; limb reattachment;
KW ischaemic reperfusion; gut infarct; myocardial infarct.
XX
OS Mammalia.
XX
PN WO200066138-A2.
XX
PD 09-NOV-2000.
XX
PF 27-APR-2000; 2000WO-US11251.
XX
PR 30-APR-1999; 99US-0302596.
XX
PA (BION-) BIONEBRASKA INC.
XX
PI Coolidge TR, Ehlers MRW;
XX
DR WPI; 2001-040881/05.
XX
PT Metabolic intervention with GLP-1 improves function of ischemic and
PT reperfused tissue -
XX
PS Disclosure; Page 11; 22pp; English.
XX
CC The present invention describes metabolic intervention with GLP-1 which
CC improves the function of ischaemic and reperfused tissue. The method for
CC amelioration of organ tissue caused by reperfusion of blood flow
CC following a period of ischaemia comprises administering a composition
CC including a compound which binds to a receptor for glucagon-like
CC peptide-1 (GLP-1), in a carrier. Also described are: (1) a method of
CC metabolic intervention with GLP-1 to improve the function of ischaemic
CC and reperfused tissue, the method comprising administering a composition
CC comprising GLP-1 in a carrier; and (2) a composition for use in the
CC metabolic intervention with GLP-1 as above. The method is useful after
CC surgical procedures selected from cardiac surgical procedures, organ
CC transplants, traumatic limb amputation and reattachment, a ischaemic
CC reperfusion event concurrent with gut infarct and myocardial infarct
CC and improves the function of ischaemic and reperfused tissues. The
CC method is devoid of side effects associated with current procedures.
CC Antigenic and immune stimulating properties are not adversely affected.
CC The present sequence represents a GLP-1 peptide which is given in the
CC exemplification of the present invention.
XX
SQ Sequence 31 AA;

AAB36428 Length: 31 January 22, 2004 18:02 Type: P Check: 7361 ..

1 HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID AAB85919 standard; peptide; 37 AA.
XX
AC AAB85919;
XX
DT 30-NOV-2001 (first entry)
XX
DE Glucagon-like peptide-1 (GLP-1) fragment (residues 1-37).
XX
KW GLP-1; organ tissue; injury; reperfusion; ischemia; glucose;
KW glucagon-like peptide-1; vasotropic; antiarrhythmic; antidiabetic.
XX
OS Mammalia.
XX
PN US6284725-B1.
XX
PD 04-SEP-2001.
XX
PF 30-APR-1999; 99US-0302596.
XX
PR 08-OCT-1998; 98US-0103498.
XX
PA (BION-) BIONEBRASKA INC.
XX
PI Coolidge TR, Ehlers MRW;
XX
DR WPI; 2001-564393/63.
XX
PT Use of glucagon-like peptide-one for amelioration of organ tissue e.g.
PT myocardium, injury after ischemia -

```
XX
PS   Disclosure; Column 8; 10pp; English.
XX
CC   The invention is directed towards the amelioration of organ tissue injury
CC   caused by reperfusion of blood flow after ischemia. The method involves
CC   administering a composition containing a compound which binds to a
CC   receptor for glucagon-like peptide-1 (GLP-1) in a carrier. GLP-1
CC   effectively enhances peripheral glucose uptake without inducing dangerous
CC   hypoglycemia. GLP-1 strongly suppresses glucagon secretion, independent
CC   of its insuliniotropic action and powerfully reduces plasma free fatty
CC   acid (FFA) level having major toxic mechanism during myocardial ischemia,
CC   substantially more than can be accomplished with insulin. The method is
CC   without side effects normally attendant with therapies presently
CC   available. GLP-1 suppresses paracrine by intra-islet release of insulin
CC   or somatostatin. GLP-1 is unique in its capacity to simultaneously
CC   stimulate insulin secretion and inhibit glucagon release. The present
CC   sequence represents a peptide fragment of mammalian GLP-1.
XX
SQ   Sequence   37 AA;

 AAB85919  Length: 37  January 22, 2004 18:02  Type: P  Check: 2897  ..

      1  HDEFERHAEG TFTSDVSSYL EGQAAKEFIA WLVKGRG

!!AA_SEQUENCE 1.0
ID   AAB85921 standard; peptide; 31 AA.
XX
AC   AAB85921;
XX
DT   30-NOV-2001  (first entry)
XX
DE   Glucagon-like peptide-1 (GLP-1) fragment (residues 7-37).
XX
KW   GLP-1; organ tissue; injury; reperfusion; ischemia; glucose;
KW   glucagon-like peptide-1; vasotropic; antiarrhythmic; antidiabetic.
XX
OS   Mammalia.
XX
PN   US6284725-B1.
XX
PD   04-SEP-2001.
XX
PF   30-APR-1999;   99US-0302596.
XX
PR   08-OCT-1998;   98US-0103498.
XX
PA   (BION-) BIONEBRASKA INC.
XX
PI   Coolidge TR,  Ehlers MRW;
XX
DR   WPI; 2001-564393/63.
XX
PT   Use of glucagon-like peptide-one for amelioration of organ tissue e.g.
PT   myocardium, injury after ischemia  -
XX
PS   Disclosure; Column 8; 10pp; English.
XX
CC   The invention is directed towards the amelioration of organ tissue injury
CC   caused by reperfusion of blood flow after ischemia. The method involves
CC   administering a composition containing a compound which binds to a
CC   receptor for glucagon-like peptide-1 (GLP-1) in a carrier. GLP-1
CC   effectively enhances peripheral glucose uptake without inducing dangerous
CC   hypoglycemia. GLP-1 strongly suppresses glucagon secretion, independent
CC   of its insuliniotropic action and powerfully reduces plasma free fatty
CC   acid (FFA) level having major toxic mechanism during myocardial ischemia,
CC   substantially more than can be accomplished with insulin. The method is
CC   without side effects normally attendant with therapies presently
CC   available. GLP-1 suppresses paracrine by intra-islet release of insulin
CC   or somatostatin. GLP-1 is unique in its capacity to simultaneously
CC   stimulate insulin secretion and inhibit glucagon release. The present
CC   sequence represents a peptide fragment of mammalian GLP-1.
XX
SQ   Sequence   31 AA;

 AAB85921  Length: 31  January 22, 2004 18:02  Type: P  Check: 7361  ..

      1  HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID   AAE32655 standard; peptide; 52 AA.
XX
AC   AAE32655;
XX
DT   24-MAR-2003  (first entry)
XX
DE   GLP-1 (7-37)-human IgG1 mutant Fc region fusion protein junction peptide.
XX
KW   Immunogenic; therapy; albumin; mutant; mutein; glucagon-like peptide-1;
KW   GLP-1 protein; Fc region; human; immunoglobulin G1; IgG1.
XX
OS   Chimeric - Homo sapiens.
OS   Chimeric - Unidentified.
XX
FH   Key             Location/Qualifiers
FT   Region          1. .31
FT                   /note= "GLP-1 (7-37) peptide"
FT   Region          32. .52
FT                   /note= "Human IgG1 Fc mutant peptide"
XX
PN   WO200279415-A2.
XX
PD   10-OCT-2002.
XX
PF   29-MAR-2002; 2002WO-US09650.
XX
PR   30-MAR-2001; 2001US-280625P.
XX
PA   (LEXI-) LEXIGEN PHARM CORP.
XX
PI   Gillies SD;
XX
DR   WPI; 2003-111794/10.
XX
PT   Reducing the immunogenicity of a fusion protein by changing an amino
PT   acid within the junction region spanning a fusion junction of a fusion
PT   protein to reduce the ability of the candidate T-cell epitope to
PT   interact with a T-cell receptor  -
XX
PS   Example 6; Page 59; 67pp; English.
XX
CC   The present invention relates to a method of reducing the immunogenicity
CC   of a fusion protein. The method involves identifying a candidate T-cell
CC   epitope within a junction region spanning a fusion junction of a fusion
CC   protein and changing an amino acid within the junction region to reduce
CC   the ability of the candidate T-cell epitope to interact with a T-cell
CC   receptor. The method is useful for reducing the immunogenicity of fusion
CC   proteins for use in therapy. The present sequence is glucagon-like
CC   peptide (GLP-1; 7-37)-human immunoglobulin G1 (IgG1) mutant Fc region
CC   fusion protein junction peptide. This sequence is used to illustrate
CC   the method of the invention.
XX
SQ   Sequence   52 AA;

 AAE32655  Length: 52  January 22, 2004 18:02  Type: P  Check: 3731  ..

      1  HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR GEPKSSDKTH TCPPCPAPEL

     51  LG

!!AA_SEQUENCE 1.0
ID   AAE32943 standard; peptide; 52 AA.
XX
AC   AAE32943;
XX
DT   24-MAR-2003  (first entry)
XX
```

DE GLP-1 (7-37)-human IgG1 mutant Fc region fusion peptide.
XX
KW T-cell; immunogenic; therapy; Fc region; fusion peptide; mutant; mutein;
KW glucagon like peptide-1; GLP-1; human; immunoglobulin G1; IgG1.
XX
OS Chimeric - Homo sapiens.
OS Chimeric - Unidentified.
XX
FH Key Location/Qualifiers
FT Region 1. .31
FT /note= "GLP-1 (7-37) peptide"
FT Region 32. .52
FT /note= "Fc mutant peptide"
XX
PN WO200279232-A2.
XX
PD 10-OCT-2002.
XX
PF 30-MAR-2002; 2002WO-US09815.
XX
PR 30-MAR-2001; 2001US-280625P.
XX
PA (LEXI-) LEXIGEN PHARM CORP.
XX
PI Gillies SD;
XX
DR WPI; 2003-103259/09.
XX
PT Reducing the immunogenicity of a fusion protein comprises changing an
PT amino acid within the junction region to reduce the ability of the
PT candidate T-cell epitope identified within the junction spanning to
PT interact with T-cell receptor -
XX
PS Example 6; Page 59-60; 68pp; English.
XX
CC The invention relates to a method for reducing the immunogenicity of a
CC fusion protein which involves identifying a candidate T-cell epitope
CC within a junction spanning a fusion junction of a fusion protein, and
CC changing an amino acid within the junction region to reduce the ability
CC of the candidate T-cell epitope to interact with a T-cell receptor. The
CC method is useful for reducing the immunogenicity of a fusion protein.
CC It is useful for analysing, changing or modifying one or more amino
CC acids in the junction region of a fusion protein to identify a T-cell
CC epitope and reduce its ability to interact with a T-cell receptor. The
CC less immunogenic fusion proteins are useful in providing therapeutic
CC treatment. The present sequence is glucagon like peptide-1 (GLP-1; 7-37)-
CC human immunoglobulin G1 (IgG1) mutant Fc region fusion peptide. This
CC peptide is used to illustrate the method of the invention.
XX
SQ Sequence 52 AA;

AAE32943 Length: 52 January 22, 2004 18:02 Type: P Check: 3731 ..

1 HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR GEPKSSDKTH TCPPCPAPEL

51 LG

!!AA_SEQUENCE 1.0
ID AAE30127 standard; peptide; 31 AA.
XX
AC AAE30127;
XX
DT 24-FEB-2003 (first entry)
XX
DE Glucagon-like peptide-1 (GLP-1).
XX
KW Immunoglobulin; Ig; antibody; immunocytokine; immunofusion; immunoligand;
KW protease resistance; glucagon-like peptide-1; GLP-1.
XX
OS Unidentified.
XX
PN WO200272605-A2.
XX
PD 19-SEP-2002.
XX
PF 07-MAR-2002; 2002WO-US07011.
XX
PR 07-MAR-2001; 2001US-274096P.
XX
PA (LEXI-) LEXIGEN PHARM CORP.
XX
PI Gillies SD, Way J;
XX
DR WPI; 2003-018726/01.
DR N-PSDB; AAD47634.
XX
PT New fusion protein, useful for producing antibodies, immunocytokines or
PT Fc fusion proteins that enhance the expression or protease resistance
PT of a fusion protein, comprises an immunoglobulin (Ig) moiety fused to a
PT non-Ig moiety -
XX
PS Example 3; Page 63; 71pp; English.
XX
CC The present invention relates to methods and compositions for efficiently
CC expressing antibody fusion proteins. The invention also relates to novel
CC fusion proteins comprising an immunoglobulin (Ig) moiety fused to a non-
CC immunoglobulin moiety where the immunoglobulin moiety comprises a first
CC domain from a first antibody isotype and a second domain from a second
CC antibody isotype. The antibodies or Ig fusion proteins are useful to
CC produce intact antibodies, immunocytokines, immunofusions, immunoligands
CC and other antibody and Fc fusion proteins that enhance the expression,
CC proper oligomerisation, purification and protease resistance of desired
CC fusion proteins, optionally with modified, combined or decreased Fc
CC effector functions. The present sequence is glucagon-like peptide-1
CC (GLP-1). This sequence is used in the exemplification of the invention.
XX
SQ Sequence 31 AA;

AAE30127 Length: 31 January 22, 2004 18:02 Type: P Check: 7361 ..

1 HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID AAE30904 standard; peptide; 31 AA.
XX
AC AAE30904;
XX
DT 24-FEB-2003 (first entry)
XX
DE Human glucagon-like peptide 1, GLP-1 (7-37) OH.
XX
KW Human; glucagon-like peptide 1; GLP-1; albumin; immunoglobulin; Ig;
KW therapy; non-insulin diabetes mellitus; obesity; antidiabetic;
KW anorectic.
XX
OS Homo sapiens.
XX
PN WO200246227-A2.
XX
PD 13-JUN-2002.
XX
PF 29-NOV-2001; 2001WO-US43165.
XX
PR 07-DEC-2000; 2000US-251954P.
XX
PA (ELIL) LILLY & CO ELI.
XX
PI Glaesner W, Micanovic R, Tschang SR;
XX
DR WPI; 2003-018534/01.
XX
PT Novel heterologous fusion protein, useful for treating non-insulin
PT dependent diabetes mellitus or obesity, comprises a glucagon-like
PT peptide 1 compound fused to human albumin or to the Fc portion of an
PT immunoglobulin -
XX

```
PS   Disclosure; Page 7; 200pp; English.
XX
CC   The invention relates to a heterologous fusion protein comprising a
CC   first polypeptide fused to a second polypeptide, where the polypeptides
CC   has a N-terminus and a C-terminus and the first polypeptide is a glucagon
CC   -like peptide 1 (GLP-1) compound and the second is a human albumin or its
CC   analogue or fragment, or the Fc portion of an immunoglobulin (Ig) or its
CC   analogue or fragment, where the C-terminus of first polypeptide is fused
CC   to the N-terminus of the second polypeptide. The invention is useful for
CC   normalising blood glucose levels in mammal, for treating a patient with
CC   non-insulin diabetes mellitus or obesity, or for the manufacture of
CC   medicament for treating the above mentioned diseases. The present
CC   sequence is human GLP-1 (7-37) OH peptide.
XX
SQ   Sequence   31 AA;

 AAE30904  Length: 31  January 22, 2004 18:02  Type: P  Check: 7361  ..

       1  HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID   AAE30916 standard; Protein; 616 AA.
XX
AC   AAE30916;
XX
DT   24-FEB-2003  (first entry)
XX
DE   Val8-GLP-1-human serum albumin (HSA) fusion protein.
XX
KW   Human; glucagon-like peptide 1; GLP-1; albumin; immunoglobulin; Ig;
KW   therapy; non-insulin diabetes mellitus; obesity; antidiabetic;
KW   anorectic; fusion protein.
XX
OS   Chimeric - Homo sapiens.
OS   Chimeric - Unidentified.
XX
PN   WO200246227-A2.
XX
PD   13-JUN-2002.
XX
PF   29-NOV-2001; 2001WO-US43165.
XX
PR   07-DEC-2000; 2000US-251954P.
XX
PA   (ELIL ) LILLY & CO ELI.
XX
PI   Glaesner W,  Micanovic R,  Tschang SR;
XX
DR   WPI; 2003-018534/01.
XX
PT   Novel heterologous fusion protein, useful for treating non-insulin
PT   dependent diabetes mellitus or obesity, comprises a glucagon-like
PT   peptide 1 compound fused to human albumin or to the Fc portion of an
PT   immunoglobulin -
XX
PS   Example 6; Page 80; 200pp; English.
XX
CC   The invention relates to a heterologous fusion protein comprising a
CC   first polypeptide fused to a second polypeptide, where the polypeptides
CC   has a N-terminus and a C-terminus and the first polypeptide is a glucagon
CC   -like peptide 1 (GLP-1) compound and the second is a human albumin or its
CC   analogue or fragment, or the Fc portion of an immunoglobulin (Ig) or its
CC   analogue or fragment, where the C-terminus of first polypeptide is fused
CC   to the N-terminus of the second polypeptide. The invention is useful for
CC   normalising blood glucose levels in mammal, for treating a patient with
CC   non-insulin diabetes mellitus or obesity, or for the manufacture of
CC   medicament for treating the above mentioned diseases. The present
CC   sequence is GLP-1 fusion protein.
XX
SQ   Sequence   616 AA;

AAE30916  Length: 616  January 22, 2004 18:02  Type: P  Check: 9940  ..

       1  HVEGTFTSDV SSYLEGQAAK EFIAWLVKGR GDAHKSEVAH RFKDLGEENF
      51  KALVLIAFAQ YLQQCPFEDH VKLVNEVTEF AKTCVADESA ENCDKSLHTL
     101  FGDKLCTVAT LRETYGEMAD CCAKQEPERN ECFLQHKDDN PNLPRLVRPE
     151  VDVMCTAFHD NEETFLKKYL YEIARRHPYF YAPELLFFAK RYKAAFTECC
     201  QAADKAACLL PKLDELRDEG KASSAKQRLK CASLQKFGER AFKAWAVARL
     251  SQRFPKAEFA EVSKLVTDLT KVHTECCHGD LLECADDRAD LAKYICENQD
     301  SISSKLKECC EKPLLEKSHC IAEVENDEMP ADLPSLAADF VESKDVCKNY
     351  AEAKDVFLGM FLYEYARRHP DYSVVLLLRL AKTYETTLEK CCAAADPHEC
     401  YAKVFDEFKP LVEEPQNLIK QNCELFEQLG EYKFQNALLV RYTKKVPQVS
     451  TPTLVEVSRN LGKVGSKCCK HPEAKRMPCA EDYLSVVLNQ LCVLHEKTPV
     501  SDRVTKCCTE SLVNRRPCFS ALEVDETYVP KEFNAETFTF HADICTLSEK
     551  ERQIKKQTAL VELVKHKPKA TKEQLKAVMD DFAAFVEKCC KADDKETCFA
     601  EEGKKLVAAS QAALGL

!!AA_SEQUENCE 1.0
ID   AAE30917 standard; Protein; 631 AA.
XX
AC   AAE30917;
XX
DT   24-FEB-2003  (first entry)
XX
DE   Val8-GLP-1-linker-human serum albumin (HSA) fusion protein.
XX
KW   Human; glucagon-like peptide 1; GLP-1; albumin; immunoglobulin; Ig;
KW   therapy; non-insulin diabetes mellitus; obesity; antidiabetic;
KW   anorectic; fusion protein.
XX
OS   Chimeric - Homo sapiens.
OS   Chimeric - Unidentified.
XX
PN   WO200246227-A2.
XX
PD   13-JUN-2002.
XX
PF   29-NOV-2001; 2001WO-US43165.
XX
PR   07-DEC-2000; 2000US-251954P.
XX
PA   (ELIL ) LILLY & CO ELI.
XX
PI   Glaesner W,  Micanovic R,  Tschang SR;
XX
DR   WPI; 2003-018534/01.
XX
PT   Novel heterologous fusion protein, useful for treating non-insulin
PT   dependent diabetes mellitus or obesity, comprises a glucagon-like
PT   peptide 1 compound fused to human albumin or to the Fc portion of an
PT   immunoglobulin -
XX
PS   Example 6; Page 80; 200pp; English.
XX
CC   The invention relates to a heterologous fusion protein comprising a
CC   first polypeptide fused to a second polypeptide, where the polypeptides
CC   has a N-terminus and a C-terminus and the first polypeptide is a glucagon
CC   -like peptide 1 (GLP-1) compound and the second is a human albumin or its
CC   analogue or fragment, or the Fc portion of an immunoglobulin (Ig) or its
CC   analogue or fragment, where the C-terminus of first polypeptide is fused
CC   to the N-terminus of the second polypeptide. The invention is useful for
CC   normalising blood glucose levels in mammal, for treating a patient with
CC   non-insulin diabetes mellitus or obesity, or for the manufacture of
CC   medicament for treating the above mentioned diseases. The present
```

```
CC   sequence is GLP-1 fusion protein.
XX
SQ   Sequence   631 AA;

AAE30917  Length: 631  January 22, 2004 18:02  Type: P  Check: 1796  ..

       1  HVEGTFTSDV SSYLEGQAAK EFIAWLVKGR GGGGGSGGGG SGGGGSDAHK

      51  SEVAHRFKDL GEENFKALVL IAFAQYLQQC PFEDHVKLVN EVTEFAKTCV

     101  ADESAENCDK SLHTLFGDKL CTVATLRETY GEMADCCAKQ EPERNECFLQ

     151  HKDDNPNLPR LVRPEVDVMC TAFHDNEETF LKKYLYEIAR RHPYFYAPEL

     201  LFFAKRYKAA FTECCQAADK AACLLPKLDE LRDEGKASSA KQRLKCASLQ

     251  KFGERAFKAW AVARLSQRFP KAEFAEVSKL VTDLTKVHTE CCHGDLLECA

     301  DDRADLAKYI CENQDSISSK LKECCEKPLL EKSHCIAEVE NDEMPADLPS

     351  LAADFVESKD VCKNYAEAKD VFLGMFLYEY ARRHPDYSVV LLLRLAKTYE

     401  TTLEKCCAAA DPHECYAKVF DEFKPLVEEP QNLIKQNCEL FEQLGEYKFQ

     451  NALLVRYTKK VPQVSTPTLV EVSRNLGKVG SKCCKHPEAK RMPCAEDYLS

     501  VVLNQLCVLH EKTPVSDRVT KCCTESLVNR RPCFSALEVD ETYVPKEFNA

     551  ETFTFHADIC TLSEKERQIK KQTALVELVK HKPKATKEQL KAVMDDFAAF

     601  VEKCCKADDK ETCFAEEGKK LVAASQAALG L

!!AA_SEQUENCE 1.0
ID   AAE30921 standard; Protein; 264 AA.
XX
AC   AAE30921;
XX
DT   24-FEB-2003  (first entry)
XX
DE   Val8-GLP-1-Immunoglobulin G1 (IgG1) fusion protein.
XX
KW   Human; glucagon-like peptide 1; GLP-1; albumin; immunoglobulin; Ig;
KW   therapy; non-insulin diabetes mellitus; obesity; antidiabetic;
KW   anorectic; fusion protein.
XX
OS   Chimeric - Homo sapiens.
OS   Chimeric - Unidentified.
XX
PN   WO200246227-A2.
XX
PD   13-JUN-2002.
XX
PF   29-NOV-2001; 2001WO-US43165.
XX
PR   07-DEC-2000; 2000US-251954P.
XX
PA   (ELIL ) LILLY & CO ELI.
XX
PI   Glaesner W,  Micanovic R,  Tschang SR;
XX
DR   WPI; 2003-018534/01.
XX
PT   Novel heterologous fusion protein, useful for treating non-insulin
PT   dependent diabetes mellitus or obesity, comprises a glucagon-like
PT   peptide 1 compound fused to human albumin or to the Fc portion of an
PT   immunoglobulin -
XX
PS   Example 6; Page 82; 200pp; English.
XX
CC   The invention relates to a heterologous fusion protein comprising a
CC   first polypeptide fused to a second polypeptide, where the polypeptides
CC   has a N-terminus and a C-terminus and the first polypeptide is a glucagon
CC   -like peptide 1 (GLP-1) compound and the second is a human albumin or its
CC   analogue or fragment, or the Fc portion of an immunoglobulin (Ig) or its
CC   analogue or fragment, where the C-terminus of first polypeptide is fused
CC   to the N-terminus of the second polypeptide. The invention is useful for
CC   normalising blood glucose levels in mammal, for treating a patient with
CC   non-insulin diabetes mellitus or obesity, or for the manufacture of
CC   medicament for treating the above mentioned diseases. The present
CC   sequence is GLP-1 fusion protein.
XX
SQ   Sequence   264 AA;

AAE30921  Length: 264  January 22, 2004 18:02  Type: P  Check: 7960  ..

       1  HVEGTFTSDV SSYLEGQAAK EFIAWLVKGR GAEPKSCDKT HTCPPCPAPE

      51  LLGGPSVFLF PPKPKDTLMI SRTPEVTCVV VDVSHEDPEV KFNWYVDGVE

     101  VHNAKTKPRE EQYNSTYRVV SVLTVLHQDW LNGKEYKCKV SNKALPAPIE

     151  KTISKAKGQP REPQVYTLPP SREEMTKNQV SLTCLVKGFY PSDIAVEWES

     201  NGQPENNYKT TPPVLDSDGS FFLYSKLTVD KSRWQQGNVF SCSVMHEALH

     251  NHYTQKSLSL SPGK

!!AA_SEQUENCE 1.0
ID   AAE30922 standard; Protein; 272 AA.
XX
AC   AAE30922;
XX
DT   24-FEB-2003  (first entry)
XX
DE   Val8-GLP-1-CEx-Immunoglobulin G1 (IgG1) fusion protein.
XX
KW   Human; glucagon-like peptide 1; GLP-1; albumin; immunoglobulin; Ig;
KW   therapy; non-insulin diabetes mellitus; obesity; antidiabetic;
KW   anorectic; fusion protein.
XX
OS   Chimeric - Homo sapiens.
OS   Chimeric - Unidentified.
XX
PN   WO200246227-A2.
XX
PD   13-JUN-2002.
XX
PF   29-NOV-2001; 2001WO-US43165.
XX
PR   07-DEC-2000; 2000US-251954P.
XX
PA   (ELIL ) LILLY & CO ELI.
XX
PI   Glaesner W,  Micanovic R,  Tschang SR;
XX
DR   WPI; 2003-018534/01.
XX
PT   Novel heterologous fusion protein, useful for treating non-insulin
PT   dependent diabetes mellitus or obesity, comprises a glucagon-like
PT   peptide 1 compound fused to human albumin or to the Fc portion of an
PT   immunoglobulin -
XX
PS   Example 6; Page 82; 200pp; English.
XX
CC   The invention relates to a heterologous fusion protein comprising a
CC   first polypeptide fused to a second polypeptide, where the polypeptides
CC   has a N-terminus and a C-terminus and the first polypeptide is a glucagon
CC   -like peptide 1 (GLP-1) compound and the second is a human albumin or its
CC   analogue or fragment, or the Fc portion of an immunoglobulin (Ig) or its
CC   analogue or fragment, where the C-terminus of first polypeptide is fused
CC   to the N-terminus of the second polypeptide. The invention is useful for
CC   normalising blood glucose levels in mammal, for treating a patient with
CC   non-insulin diabetes mellitus or obesity, or for the manufacture of
CC   medicament for treating the above mentioned diseases. The present
CC   sequence is GLP-1 fusion protein.
XX
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SQ   Sequence   272 AA;

AAE30922  Length: 272  January 22, 2004 18:02  Type: P  Check: 5244  ..

       1  HVEGTFTSDV SSYLEGQAAK EFIAWLVKGR GSSGAPPPSA EPKSCDKTHT

      51  CPPCPAPELL GGPSVFLFPP KPKDTLMISR TPEVTCVVVD VSHEDPEVKF

     101  NWYVDGVEVH NAKTKPREEQ YNSTYRVVSV LTVLHQDWLN GKEYKCKVSN

     151  KALPAPIEKT ISKAKGQPRE PQVYTLPPSR EEMTKNQVSL TCLVKGFYPS

     201  DIAVEWESNG QPENNYKTTP PVLDSDGSFF LYSKLTVDKS RWQQGNVFSC

     251  SVMHEALHNH YTQKSLSLSP GK

!!AA_SEQUENCE 1.0
ID   AAE30953 standard; peptide; 31 AA.
XX
AC   AAE30953;
XX
DT   24-FEB-2003  (first entry)
XX
DE   Human GLP/exendin peptide analogue #17.
XX
KW   Human; glucagon-like peptide 1; GLP-1; albumin; immunoglobulin; Ig;
KW   therapy; non-insulin diabetes mellitus; obesity; antidiabetic;
KW   anorectic.
XX
OS   Homo sapiens.
XX
PN   WO200246227-A2.
XX
PD   13-JUN-2002.
XX
PF   29-NOV-2001; 2001WO-US43165.
XX
PR   07-DEC-2000; 2000US-251954P.
XX
PA   (ELIL ) LILLY & CO ELI.
XX
PI   Glaesner W,  Micanovic R,  Tschang SR;
XX
DR   WPI; 2003-018534/01.
XX
PT   Novel heterologous fusion protein, useful for treating non-insulin
PT   dependent diabetes mellitus or obesity, comprises a glucagon-like
PT   peptide 1 compound fused to human albumin or to the Fc portion of an
PT   immunoglobulin -
XX
PS   Example 6; Page 91; 200pp; English.
XX
CC   The invention relates to a heterologous fusion protein comprising a
CC   first polypeptide fused to a second polypeptide, where the polypeptides
CC   has a N-terminus and a C-terminus and the first polypeptide is a glucagon
CC   -like peptide 1 (GLP-1) compound and the second is a human albumin or its
CC   analogue or fragment, or the Fc portion of an immunoglobulin (Ig) or its
CC   analogue or fragment, where the C-terminus of first polypeptide is fused
CC   to the N-terminus of the second polypeptide. The invention is useful for
CC   normalising blood glucose levels in mammal, for treating a patient with
CC   non-insulin diabetes mellitus or obesity, or for the manufacture of
CC   medicament for treating the above mentioned diseases. The present
CC   sequence is human GLP/exendin peptide analogue.
XX
SQ   Sequence   31 AA;

 AAE30953  Length: 31  January 22, 2004 18:02  Type: P  Check: 7403  ..

       1  HVEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID   AAE30954 standard; peptide; 31 AA.
XX
AC   AAE30954;
XX
DT   24-FEB-2003  (first entry)
XX
DE   Human GLP/exendin peptide analogue #18.
XX
KW   Human; glucagon-like peptide 1; GLP-1; albumin; immunoglobulin; Ig;
KW   therapy; non-insulin diabetes mellitus; obesity; antidiabetic;
KW   anorectic.
XX
OS   Homo sapiens.
XX
PN   WO200246227-A2.
XX
PD   13-JUN-2002.
XX
PF   29-NOV-2001; 2001WO-US43165.
XX
PR   07-DEC-2000; 2000US-251954P.
XX
PA   (ELIL ) LILLY & CO ELI.
XX
PI   Glaesner W,  Micanovic R,  Tschang SR;
XX
DR   WPI; 2003-018534/01.
XX
PT   Novel heterologous fusion protein, useful for treating non-insulin
PT   dependent diabetes mellitus or obesity, comprises a glucagon-like
PT   peptide 1 compound fused to human albumin or to the Fc portion of an
PT   immunoglobulin -
XX
PS   Example 6; Page 91; 200pp; English.
XX
CC   The invention relates to a heterologous fusion protein comprising a
CC   first polypeptide fused to a second polypeptide, where the polypeptides
CC   has a N-terminus and a C-terminus and the first polypeptide is a glucagon
CC   -like peptide 1 (GLP-1) compound and the second is a human albumin or its
CC   analogue or fragment, or the Fc portion of an immunoglobulin (Ig) or its
CC   analogue or fragment, where the C-terminus of first polypeptide is fused
CC   to the N-terminus of the second polypeptide. The invention is useful for
CC   normalising blood glucose levels in mammal, for treating a patient with
CC   non-insulin diabetes mellitus or obesity, or for the manufacture of
CC   medicament for treating the above mentioned diseases. The present
CC   sequence is human GLP/exendin peptide analogue.
XX
SQ   Sequence   31 AA;

 AAE30954  Length: 31  January 22, 2004 18:02  Type: P  Check: 7361  ..

       1  HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

!!AA_SEQUENCE 1.0
ID   AAE31010 standard; peptide; 31 AA.
XX
AC   AAE31010;
XX
DT   24-FEB-2003  (first entry)
XX
DE   Human GLP-1 analogue, Val8-GLP-1(7-37) OH.
XX
KW   Human; glucagon-like peptide 1; GLP-1; albumin; immunoglobulin; Ig;
KW   therapy; non-insulin diabetes mellitus; obesity; antidiabetic;
KW   anorectic; mutant; mutein.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 2
FT                   /note= "Wild type Ala substituted with Val"
XX
PN   WO200246227-A2.
XX
```

PD 13-JUN-2002.
XX
PF 29-NOV-2001; 2001WO-US43165.
XX
PR 07-DEC-2000; 2000US-251954P.
XX
PA (ELIL) LILLY & CO ELI.
XX
PI Glaesner W, Micanovic R, Tschang SR;
XX
DR WPI; 2003-018534/01.
XX
PT Novel heterologous fusion protein, useful for treating non-insulin
PT dependent diabetes mellitus or obesity, comprises a glucagon-like
PT peptide 1 compound fused to human albumin or to the Fc portion of an
PT immunoglobulin -
XX
PS Example 6; Page -; 200pp; English.
XX
CC The invention relates to a heterologous fusion protein comprising a
CC first polypeptide fused to a second polypeptide, where the polypeptides
CC has a N-terminus and a C-terminus and the first polypeptide is a glucagon
CC -like peptide 1 (GLP-1) compound and the second is a human albumin or its
CC analogue or fragment, or the Fc portion of an immunoglobulin (Ig) or its
CC analogue or fragment, where the C-terminus of first polypeptide is fused
CC to the N-terminus of the second polypeptide. The invention is useful for
CC normalising blood glucose levels in mammal, for treating a patient with
CC non-insulin diabetes mellitus or obesity, or for the manufacture of
CC medicament for treating the above mentioned diseases. The present
CC sequence is human GLP-1 (7-37) OH peptide analogue.
CC Note: This sequence is not shown in the specification, however it is
CC constructed based on human GLP-1 (7-37) OH peptide sequence shown as
CC SEQ ID NO:1 (AAE30904) in page 7 of the specification.
XX
SQ Sequence 31 AA;

AAE31010 Length: 31 January 22, 2004 18:02 Type: P Check: 7403 ..

1 HVEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

||AA_SEQUENCE 1.0
ID AAE31011 standard; peptide; 31 AA.
XX
AC AAE31011;
XX
DT 24-FEB-2003 (first entry)
XX
DE Human GLP-1 analogue, Gly8-GLP-1(7-37) OH.
XX
KW Human; glucagon-like peptide 1; GLP-1; albumin; immunoglobulin; Ig;
KW therapy; non-insulin diabetes mellitus; obesity; antidiabetic;
KW anorectic; mutant; mutein.
XX
OS Homo sapiens.
OS Synthetic.
XX
FH Key Location/Qualifiers
FT Misc-difference 2
FT /note= "Wild type Ala substituted with Gly"
XX
PN WO200246227-A2.
XX
PD 13-JUN-2002.
XX
PF 29-NOV-2001; 2001WO-US43165.
XX
PR 07-DEC-2000; 2000US-251954P.
XX
PA (ELIL) LILLY & CO ELI.
XX
PI Glaesner W, Micanovic R, Tschang SR;
XX
DR WPI; 2003-018534/01.
XX
PT Novel heterologous fusion protein, useful for treating non-insulin
PT dependent diabetes mellitus or obesity, comprises a glucagon-like
PT peptide 1 compound fused to human albumin or to the Fc portion of an
PT immunoglobulin -
XX
PS Claim 80; Page -; 200pp; English.
XX
CC The invention relates to a heterologous fusion protein comprising a
CC first polypeptide fused to a second polypeptide, where the polypeptides
CC has a N-terminus and a C-terminus and the first polypeptide is a glucagon
CC -like peptide 1 (GLP-1) compound and the second is a human albumin or its
CC analogue or fragment, or the Fc portion of an immunoglobulin (Ig) or its
CC analogue or fragment, where the C-terminus of first polypeptide is fused
CC to the N-terminus of the second polypeptide. The invention is useful for
CC normalising blood glucose levels in mammal, for treating a patient with
CC non-insulin diabetes mellitus or obesity, or for the manufacture of
CC medicament for treating the above mentioned diseases. The present
CC sequence is human GLP-1 (7-37) OH peptide analogue.
CC Note: This sequence is not shown in the specification, however it is
CC constructed based on human GLP-1 (7-37) OH peptide sequence shown as
CC SEQ ID NO:1 (AAE30904) in page 7 of the specification.
XX
SQ Sequence 31 AA;

AAE31011 Length: 31 January 22, 2004 18:02 Type: P Check: 7373 ..

1 HGEGTFTSDV SSYLEGQAAK EFIAWLVKGR G

||AA_SEQUENCE 1.0
ID AAO19585 standard; peptide; 37 AA.
XX
AC AAO19585;
XX
DT 13-FEB-2003 (first entry)
XX
DE Mammalian GLP-1(1-37).
XX
KW Mammal; GLP-1; glucagon-like peptide-1; insulin resistance; diabetes;
KW atherosclerotic cardiovascular disease; congestive heart failure;
KW antidiabetic; antiarteriosclerotic; cardiant.
XX
OS Mammalia.
XX
PN WO200285406-A1.
XX
PD 31-OCT-2002.
XX
PF 24-APR-2002; 2002WO-US13088.
XX
PR 24-APR-2001; 2001US-285699P.
XX
PA (REST-) RESTORAGEN INC.
XX
PI Holst JJ, Olsen MZ, Hathaway DR;
XX
DR WPI; 2003-046959/04.
XX
PT Treatment of insulin resistance-associated conditions, e.g. type-2
PT pre-diabetes, ASCD, drug-induced insulin resistance, congestive heart
PT failure or diminished exercise capacity, comprises administration of
PT GLP-1 -
XX
PS Disclosure; Page 10; 60pp; English.
XX
CC The present invention relates to a method of treating insulin
CC resistance-associated conditions comprising administration of
CC glucagon-like peptide-1 (GLP-1). The method is useful for treating
CC insulin resistance-associated conditions, especially type-2 pre-diabetes,
CC atherosclerotic cardiovascular diseases (ASCD), drug-induced insulin
CC resistance (especially glucocorticoid- or growth hormone-induced),
CC congestive heart failure (not associated with toxic hypervolemia),
CC diminished exercise capacity of skeletal muscle and left ventricular

CC dysfunction with cardiac metabolic myopathy or diminished exercise
CC capacity of skeletal muscle. The present sequence is a mammalian GLP-1
CC peptide.
XX
SQ Sequence 37 AA;

AA019585 Length: 37 January 22, 2004 18:02 Type: P Check: 2897 ..

1 HDEFERHAEG TFTSDVSSYL EGQAAKEFIA WLVKGRG

!!AA_SEQUENCE 1.0
ID AA019587 standard; peptide; 31 AA.
XX
AC AA019587;
XX
DT 13-FEB-2003 (first entry)
XX
DE Mammalian GLP-1(7-37).
XX
KW Mammal; GLP-1; glucagon-like peptide-1; insulin resistance; diabetes;
KW atherosclerotic cardiovascular disease; congestive heart failure;
KW antidiabetic; antiarteriosclerotic; cardiant.
XX
OS Mammalia.
XX
PN WO200285406-A1.
XX
PD 31-OCT-2002.
XX
PF 24-APR-2002; 2002WO-US13088.
XX
PR 24-APR-2001; 2001US-285699P.
XX
PA (REST-) RESTORAGEN INC.
XX
PI Holst JJ, Olsen MZ, Hathaway DR;
XX
DR WPI; 2003-046959/04.
XX
PT Treatment of insulin resistance-associated conditions, e.g. type-2
PT pre-diabetes, ASCD, drug-induced insulin resistance, congestive heart
PT failure or diminished exercise capacity, comprises administration of
PT GLP-1 -
XX
PS Disclosure; Page 10; 60pp; English.
XX
CC The present invention relates to a method of treating insulin
CC resistance-associated conditions comprising administration of
CC glucagon-like peptide-1 (GLP-1). The method is useful for treating
CC insulin resistance-associated conditions, especially type-2 pre-diabetes,
CC atherosclerotic cardiovascular diseases (ASCD), drug-induced insulin
CC resistance (especially glucocorticoid- or growth hormone-induced),
CC congestive heart failure (not associated with toxic hypervolemia),
CC diminished exercise capacity of skeletal muscle and left ventricular
CC dysfunction with cardiac metabolic myopathy or diminished exercise
CC capacity of skeletal muscle. The present sequence is a mammalian GLP-1
CC peptide.
XX
SQ Sequence 31 AA;

AA019587 Length: 31 January 22, 2004 18:02 Type: P Check: 7361 ..

1 HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR G